Digitized by the Internet Archive
in 2018 with funding from
University of Toronto

https://archive.org/details/medjournalApr1936uoft

THE UNIVERSITY OF TORONTO MEDICAL JOURNAL

(An Undergraduate Publication)

This journal is published seven times a year, November to May, by the Medical Society of the University of Toronto, to serve as a medium for student expression and to bring to the student recent articles of scientific interest.

STAFF ADVISOR
Prof. E. A. Linell, M.B., Ch.B., M.D. Manc.

EDITOR-IN-CHIEF
O. M. Solandt, M.A., B.Sc. (Med.) '36.

ASSISTANT EDITOR
Hugh Hayward, B.A., '37.

ASSOCIATE EDITORS
Miss J. F. Davey, B.A., '36.
B. H. McNeel, B.A., '36.
J. P. Fletcher, M.A., '37.
W. G. Bigelow, B.A., '38.

MANAGING EDITOR
Hugh J. Bright, '36.

ASSISTANT MANAGING EDITOR
A. W. Sturgeon, '37.

YEAR REPRESENTATIVES
D. D. Bonnycastle, '36.
B. T. Rogers, '37.
B. W. Vale, '38.
V. R. Perry, '39.
R. I. Probert, '40.
V. V. Marinelli, '41.

EDITOR IN CHARGE OF THIS ISSUE
W. G. Bigelow, B.A.

Address all communications to Room 107, Anatomy Building.

Volume XIII | TORONTO, APRIL, 1936 | Number 6

EDITORIAL

The majority of graduates in Medicine eventually go into "general practice," and it would, therefore, seem logical to train them for that special branch of the art. With the present system of medical education, in which clinical experience is confined to hospiital practice, it is inevitable that almost all the teaching is done by specialists. Each teacher is eminently fitted to instruct the students in the intricacies of his chosen field, but very often, in spite of his best efforts, he fails to teach the subject from the point of view of the general practitioner. The teaching in the Out-Patients' Department is the closest approach to general practice which is possible in a hospital, but even it does not exactly duplicate the problems which perplex the average doctor. Since it is not possible, or even desirable to have the teaching done by general practitioners, it would seem best to try to give the student some appreciation of the viewpoint of the family physician early in his clinical training. He will then understand the type of knowledge and skill that he will require in practice and will be able to direct his efforts toward obtaining it.

We wonder if experience in general practice could not be easily obtained for

any students who desire it. Already a few doctors in the city are finding that a student can be very useful in obstetrical work and not infrequently send for a student to assist them. This plan might be extended by establishing a registry where doctors who wished to have a student assistant in the summer or at other times might apply. Many students would be only too glad to have the opportunity of actually seeing the type of work which the general practitioner is called upon to do. Such an arrangement would, of course, be quite optional and both student and doctor would be free to terminate the temporary partnership whenever they wished. We feel that some such plan deserves a trial and that it would prove to be of real value to both doctors and students.

———

THE REVISED CONSTITUTION OF THE MEDICAL JOURNAL

On page 214 is to be found a copy of the new Constitution of this journal.

For 13 years the Journal has maintained a fairly uniform standard, but has not shown the growth and improvement that might be expected of the Journal of such an active medical school. It was felt that lack of general interest in the Journal and lack of funds were the two chief hindrances to progress. We hope that the new Constitution will remove these two stumbling blocks and result in the rapid expansion of the Journal. The finances should benefit, not only by the added income from subscriptions, but by increased advertising resulting from the wider circulation of the Journal. The distribution of the Journal to every student should increase student interest in it and also encourage the students to feel that it is their Journal and that they are, in some measure, responsible for its success or failure. The provision of a larger Advisory Staff from the Faculty will undoubtedly aid in maintaining or better in raising, the standards of the material printed.

The Staff of the Journal are very grateful to the many students who supported the revision of the Constitution at the annual elections. We feel sure that the future progress of the Journal will justify the changes that have been made.

———

BOOKS

An increasing number of book agents are attempting to sell medical books directly to students. In many cases, the books are sent on approval and payments are arranged in easy instalments. Many students have recently found that it is far easier to get books on approval than it is to return them later. The agent who was so affable when arranging for the delivery of the books becomes very disagreeable when the return of the books is suggested. Much unpleasantness can be avoided by refusing to accept any books on approval. If the books are of any real value, they will be found in one or other of the local libraries, where they can be examined to see if they are worth buying.

ERRATA

We greatly regret that several errors were made in the printing of Dr. F. O. Wishart's paper on Virus Diseases of Man in our February issue. The following corrections should be noted. Page 120, column 1, 11th line from the bottom, should read, "such a classification has obvious disadvantages." Page 121, column 2, insert before the seventh line from the bottom, "Since measles may be controlled in this way, it is necessary—." Page 122, under the heading, "Influenza," the third and fourth lines should read, "—causation of influenza has been obtained. A febrile disease has been transmitted in series in ferrets and—"

BUERGER'S DISEASE

By J. HAROLD COUCH, M.D.

The fact that we really understand so little about Buerger's disease supplies a constant incentive for its further study. If, however, this incentive were not sufficient, the apparently increasing incidence of this most disabling affliction among us would compel attention and study. Treatment heretofore, has been empirical and directed toward the relief of gross symptoms rather than toward the correction of the fundamental underlying faults. More recently, however, workers with a biochemical turn of mind have been directing their attention to this study and it may be that we now have a therapy which does tend to correct the essential physiological aberrations responsible for this disease. For the sake of brevity and clearness, dogmatic statements may be made in this article without seeming to have sufficient support. The support, however, is available. It should further be stated that some of the views herein expressed do not represent the unanimous opinion of all the surgeons interested in this disease, but rather, are views for which the author alone accepts responsibility.

Definition.

Buerger's disease has been defined as a sterile inflammation involving the walls of the arteries and veins of the extremities and characterized by interrupted progress to ultimate thrombosis and gangrene. But thoughtful workers everywhere are dissatisfied with this definition which leaves unexplained many of the essential features of the disease.

A more complete definition might be suggested—Buerger's disease is an hereditary sex-linked disease confined to males, characterized by a concentration of the blood and having as its more obvious manifestations, inflammation of the vessels of the extremities with consequent thrombosis and gangrene.

Pathology.

The obvious pathology has been well and often described. The artery and vein wall and even the whole neurovascular bundle are involved in a sterile inflammatory process with resultant fibrosis, matting them tightly together, a thickening of the wall produces narrowing of the lumen of the vessels and finally thrombosis occurs with impaired circulation to the extremities beyond, the evidences of which are clearly seen. During the time that the main circulation is gradually becoming inadequate, a collateral circulation is being developed which may be able to carry on a nourishing of the foot for some time.

The less obvious, though more essential, pathological changes characteristic of Buerger's disease, have more recently been described and consist of a chronic dehydration or concentration of the blood stream with consequent chemical imbalance. The evidence of these changes are set forth by various workers of which one or two may be named.

Rabinowitz, of Montreal, in an article entitled, "Newer Concepts in Physiopathology and Treatment of Thrombo-Angitis Obliterans," has described a profound upset in the lecithin metabolism and content of the blood stream associated with Buerger's disease and not found in normal controls. Silbert, at Mount Sinai Hospital, New York, has demonstrated that in Buerger's disease, the total blood volume is reduced by as much as twenty-five per cent. of the normal, so that these people have only three-quarters as much fluid blood per kilo body weight as normal. Further evidence of the concentration of blood is found in an increased concentration of the solid constituents of blood by a corresponding amount. Total ash content, mineral content are twenty-five per cent. more concentrated than usual. An increased viscosity, increased haemo-

globin content and an increased red blood count are also consistently present. These findings are constant for Buerger's disease and are not found in any other disease.

Signs and Symptoms.

The obvious signs and symptoms on which the diagnosis of Buerger's disease is made are associated chiefly with the impaired circulation of the extremities.

1. **Coldness**: Patients with early Buerger's disease complain only of coldness of the feet, made worse by exposure to dampness or by standing outdoors. They complain also of inability to get their feet warm in bed at night, particularly in the winter time. Not everyone with cold feet has Buerger's disease.

2. **Fatigue**: Fatigue is located in the muscles of the foot or in the muscles of the leg or calf. It is experienced after seemingly inadequate exercise and the patient himself is aware that it is progressive.

3. **Colour Change**: The characteristic colour changes found in Buerger's disease are very clear. On hanging the leg in a dependent position, the toes and foot, for a varying distance up, become deep bluish red or plum colour. On elevating the foot above the body, the skin becomes unduly blanched and takes on a white waxy appearance. The patient may complain of pain either when the foot is dependent and becomes engorged with blood or when it is elevated and becomes drained of blood.

4. **Claudication**: Patients observe a steady decrease in the distance they can walk before being stopped by pain which is located either on the dorsum of the foot, up the shin, or in the calf of the leg. It is not uncommon to find a patient whose distance is gradually cut down until finally he can walk only half a block, at the end of which time he is forced to stop and stand still on the street for a few minutes until the pain of claudication disappears, permitting him to continue for another half block. This pain of intermittent claudication is probably due to anoxaemia of muscle, in which respect it resembles the intermittent claudication of arteriosclerosis or angina pectoris.

5. **Rest Pain**: As the disease progresses, a stage is reached in which the patient complains of pain not brought on by exertion, but present even while lying still at rest in bed. This is a bad omen and usually means impending gangrene. The exact mechanism of its production is not understood.

6. **Diminished Pulsation**: On examination of the peripheral vessels, diminished or absent pulsation will be noted. The dorsalis pedis and posterior tibial arteries commonly cannot be felt to pulsate and in many cases, even the popliteal pulsation is absent. At this stage, the well-being of the foot beyond depends on collateral circulation.

7. **Migratory thrombo - phlebitis**: Migratory thrombo-phlebitis is found only in about one-third of the cases of Buerger's disease, but when found is pathognomonic of the disease. It is characterized by patches of redness, tenderness and pain appearing suddenly. If, in a true case of Buerger's, biopsy be made and the veins involved in the thrombo-phlebitis at this stage be removed, the pathologist's report will be "Buerger's Disease." The picture is characteristic.

8. **Gangrene**: Gangrene of Buerger's disease involves usually the toes or dorsum of foot. It appears rather more suddenly than does the gangrene of arteriosclerosis, being due often in the final stages to a sudden thrombosis of vessels, which have up to the moment been nourishing this part, even though poorly.

Prognosis:

The prognosis in Buerger's disease is bad. The disease is progressive to ultimate thrombosis, gangrene and loss of legs. It progresses, however, interruptedly, being characterized by remissions and crises. The cardinal signs of ill-omen suggesting rapid progress and early amputation are three: (1) *Rest Pain*: A patient who suffers not only intermittent claudication, but pain in the foot, even while in bed at rest, is faced with a gloomy future. This pain is

usually indicative of early gangrene. (2) *Loss of Popliteal Pulsation*: If pulsation in popliteal artery cannot be felt, it is an indication that the disease is extensive in its distribution involving the main-named arteries well up into the leg, as high, in fact, as the popliteal space. This naturally augurs ill for the leg beyond and the prospect of early amputation is unavoidable. (3) *Gangrene*: The presence of gangrene, no matter how small, is an indication that already the nourishment to the foot is failing and amputation is imminent. The converse of these three is also fortunately true. The patient who has no gangrene, has no rest pain, and whose popliteal pulsation can be felt, may be regarded as a hopeful case who should be encouraged to persist in treatment, for the outlook is good and he can be restored to normal usefulness in the community for an indefinite period of time, provided he follows the rules.

Causes of Buerger's Disease:

The exact cause of Buerger's disease is not known. There are, however, two factors which are responsible for its appearance. The first may be called a predisposing cause, and the second, a precipitating cause.

(1) **Predisposing Cause:** The predisposing cause of Buerger's disease is the inheritance of a nervous mechanism or a vascular mechanism, including the blood stream itself, which is capable of the changes characteristic of Buerger's disease, providing that the adequate precipitating cause is forthcoming. This hereditary factor explains the appearance of Buerger's disease in males only. The modern emancipated female who smokes perhaps more than her brother, need not fear Buerger's disease, for no woman will get Buerger's disease, no matter how much she smokes; just as no woman will bleed to death from hemophilia, no matter how often she cut herself

The hereditary factor also explains the fact that many men may smoke heavily and yet not get the disease, for a man who has not inherited the type of nervous and vascular system capable of Buerger's disease, will not get the disease, no matter how much he smokes. Conversely, Silbert states that he has never seen the true typical, proven Buerger's disease in a man who did not smoke.

(2) **Precipitating Cause:** The previous paragraph leads us, obviously, to the discussion of the precipitating cause of Buerger's disease, which is smoking of cigarettes.

It is quite possible and even probable that as a result of some of the studies now under way, other precipitating causes may yet be found and this further information may point the way to other and more logical forms of treatment.

Evidence in Support of Smoking as a Precipitating Cause:

For many years, writers all over the world have called attention to the seeming correlation between the use of tobacco, particularly in the form of cigarettes, and the appearance of Buerger's disease. The relationship has not been close nor clear. For many years, we have stumbled over the fact that many men who smoke do not acquire Buerger's disease and that among women, with whom smoking is becoming increasingly prevalent, until now many even smoke because they enjoy it, Buerger's disease does not occur. It has been pointed out above that these facts are not at all incompatible with the statement that tobacco is the precipitating cause of Buerger's disease. The weight of evidence is now so great, and the number of observers so many, that the correlation between the use of tobacco and the incidence of Buerger's disease, can no longer be dismissed with a smile.

A few references will suffice to support this conclusion: First, the Mayo clinic, who are not primarily supporters of the smoking theory, found themselves compelled to admit that their greatest incidence of amputation was among heavy smokers. They classify smokers, as they do all other things, into four

groups: (1) Non, (2) Mild, (3) Moderate, (4) Severe. Their highest incidence of amputations occurred in group four, namely, heavy smokers. In the second place, Walter Maddock, of Ann Arbor, Michigan, has shown that the inhalation of cigarette smoke causes vaso-spasm in normal individuals, while the inhalation of smoke from control cigarettes containing no tobacco, does not cause vaso-spasm. In the third place, Samuel Silbert, Mount Sinai Hospital, New York, states in most forceful language that he considers the smoking of cigarettes the one and only precipitating cause of Buerger's disease. He says that he has never seen a proven typical case of Buerger's disease in a non-smoker and he has seen in the neighbourhood of 1,000 cases. Moreover, his relapses or failures of treatment have occurred in people who resume smoking, even after having been warned. So strongly does he feel on this score that he regards the cessation of smoking as a *sine qua non* of treatment and refuses to continue with the treatment of patients who refuse to co-operate to this extent. Fourthly, in conversation, several of our friends observed the production of vaso-spasm in themselves, caused by smoking. One member of the surgical staff observed that since giving up smoking, his fingers no longer become white and painful when driving his car in cold winter weather. Another member of the staff observes that the use of cigarettes in excess causes him to have definite sub-sternal feeling of tightness and distress. Without wishing to play on the word, we feel justified in suggesting that "where there is so much smoke, there must be some fire."

Treatment:

The multiplicity of treatments bespeaks their inadequacy. Many forms of treatments have been suggested for Buerger's disease in the past. Some are ingenious and clever; some are not. We may mention a few of them only.

1. **Contrast Baths:** Contrast baths consist in immersing the feet first in hot water, then in ice-cold water, alternating until vigorous circulation is worked up. This undoubtedly will produce a certain amount of hyperemia and will carry the patient along for a little time, giving relief in cases not too far advanced. It depends for this result on the facility of the collateral circulation.

2. **Exercises:** The "daily dozen" fills this bill. The feet are elevated over the head for so many seconds, then allowed to hang in a dependent position for so many seconds. This is done, more or less faithfully, by the patient each night and morning. Once again, the results obtained in some cases are dependent on the ability of the collateral circulation to respond to changes in demand

3. **Artificial Fever:** The production of artificial fever by various vaccines, typhoid, foreign protein injection, such as milk, or the injection of sulphur has resulted in some cases in rather doubtful relief.

4. **Pavaex:** The use of the glass boot, or pavaex, as it is called, in which the foot is subjected to increases and decreases in pressure above and below atmospheric pressure. with the resultant engorgement and depletion of blood supply, has recently been suggested in treatment of Buerger's disease. It undoubtedly has a place in tiding a patient over a threatened or impending gangrene until the collateral circulation can take over the new demands made upon it and supply the parts with sufficient blood to carry on, or until amputation has been arranged.

5. **Peri-arterial Sympathectomy:** Peri-arterial sympathectomy has been advocated by the followers of Lariche. It consists in baring the femoral artery and dissecting off the adventitia together with its plexus of sympathetic nerves. This is said to result in a dilatation of the vessel beyond the point of operation with consequent enrichment of blood supply to the distal parts. This may be true, inasmuch as it takes no account of the anatomy of the sympathetic nervous system in its peripheral distribution. Sympathetic nerves, after leaving the sympathetic trunk, run with sensory somatic nerves for varying distances

leaving the nerve at irregular points in its course and travelling in long sloping paths to reach the blood vessel, where they are finally distributed in the wall acting as vasoconstrictors. A peri-arterial sympathectomy, therefore, may leave the sympathetic innervation of the vessel below that point unaltered.

6. **Lumbar Sympathectomy**: The removal of the whole lumbar sympathetic chain, leaving the vasodilators distal to that point unopposed, has undoubtedly a place in the treatment of a patient suffering from Buerger's disease, if not in the treatment of Buerger's disease itself. When we consider that Buerger's disease is a chronic dehydration or concentration of the blood with biochemical imbalances, and that even its grossest manifestations are inflammation of blood vessel wall with thrombosis and distal gangrene and when we consider further that lumbar sympathectomy removes the vasoconstrictors and leaves the vasodilators unopposed, it is obvious that lumbar sympathectomy does not alter, in the slightest degee, the pathological processes going on in a patient suffering from Buerger's disease. It does, however, have a very valuable place in the treatment of impending or early gangrene, due to any cause at all, whether it be Buerger's disease or arteriosclerosis, and it depends for its successful action on the vaso-dilation obtained in the uninvolved and tolerant collateral bed rather than any vaso-dilitation obtained in the main trunks which are involved in a serious and destructive process. This is the reason it is successful in arteriosclerosis as well.

7. **Stop Smoking**: This treatment, of which Silbert is the chief proponent, is so simple and common sense that it appeals to neither patient nor doctor. It has, however, the one slight advantage that it avoids cutting off legs. It is divided into two parts. The first part consists of nothing more or less than an application of the old therapeutic saw, namely, "remove the cause." If the precipitating cause of Buerger's disease is the smoking of cigarettes, then the treatment of Buerger's disease is the banishment of cigarettes, for that particular patient. This simple procedure cannot be too strongly urged, for without it no cure is possible, and yet we find again and again, a tendency among patients and doctors to become blinded by the glamour of the "saline treatment" and to look for remarkable results from the injection of hypertonic saline, regardless of whether or not the first step of the treatment is carried out. A patient who will not stop smoking should immediately be discharged. There is no use wasting time or saline on him. Once, however, the co-operation of the patient has been obtained, to this extent, the second step of the treatment may be entered into and it will be found to be simplicity itself. The details consist simply in the intravenous injection of 300 cubic centimetres of 5% saline three times a week for a month, twice a week for a month, once a week for a month, and once a month for six months.

Advantages of Non-Smoking and Saline Treatment:

The great advantage of this form of treatment are, first, that it applies a logical principle, and, second, that it seems to attack the altered processes found in these people. As stated above, the first and most important step is the removal of the cause. The banishment of smoking arrests the progress of Buerger's disease. In the second place, however, the intravenous injection of hypertonic saline is the only treatment suggested to date which seems to correct the fundamental underlying faults apparently responsible for the manifestations of Buerger's disease. By this means, and by this means only, has it been possible to restore the blood volume and viscosity of these patients approximately to normal. The evidence of the increase in blood volume may be found in the chain of findings which follow treatment. Immediately on the intravenous introduction of the hypertonic saline, the patient complains of feeling hot and flushed, mouth dry, salty taste, throbbing in temples, cramps in abdomen.

Further investigation will reveal a fall of the red blood cells from somewhere in the neighbourhood of five million to four and a half million, and a corresponding fall in haemoglobin of somewhere in the neighbourhood of twenty points. These changes come on within a few minutes. They are, however, more or less permanent over a period of time and further detailed investigation reveals that the obscure biochemical aberrations, associated with this disease are restored to a semblance of normal during the course of this treatment. Blood volume, total ash content, viscosity, mineral content, basal metabolic rate, all tend to return to within normal limit. Pulsation which has been absent in arteries of the extremities will even be found to have returned. Pain disappears, ulcerations heal, gangrenous process is arrested and progresses no further. The strange part of it is that once having been established, these changes seem to be permanent so long as the patient refrains strictly from the use of cigarettes. They will, however, be re-initiated by any fall from grace.

Disadvantages of Non-Smoking and Saline Treatment:

This treatment is not without some disadvantages. In the first place, it is not nearly so dramatic as a surgical operation. For this reason, it does not impress itself upon the patient, or the public. In the second place, it is more of a nuisance to the surgeon than any surgical operation. It means faithful intavenous administrations of the saline at frequent intervals, instead of an operation, which is completed and over with. In the third place, the hospitalization of the patient is necessary for a time, perhaps longer than that required for operation. He should be in hospital for at least the first month of treatment, during which time intravenous injections must be carried out three times a week. Preferably he should be in hospital for the first two months. Fourth, the time element is of some serious consideration. These patients must be under treatment for anywhere from three months to three years, and the faithful adherance to treatment during all this time requires a certain amount of moral fortitude on the part of both patient and surgeon. Fifthly, very many Buerger's patients indeed, are extremely loath to give up cigarettes. It seems that the pain of Buerger's disease drives them to the use of cigarettes as a solace and many times a patient on the ward, will be found sitting up wide awake in the middle of the night, smoking cigarettes. The late Harold Webber, whose tragic end was recently reported in our daily press, is a pathetic illustration of this fact. Only a few weeks ago, he was seen by the author at the Out-Patients' Department, Toronto General Hospital, a young man of twenty-six, sitting in a wheel chair with both legs amputated above the knee, terrified almost to the point of panic, because he himself recognized the early manifestations of the same dread process in his nicotine-stained fingers and knew that it was only a matter of time until he would lose his hands. He pleaded for some words of encouragement, "Doctor, I would do anything you say to get better," and then added with a smile, "except give up smoking."

Evidence of Efficacy of Treatment:

Buerger's disease is a disease characterized by remission. It is, therefore, very difficult to estimate the value of any form of treatment. A patient may pass into a natural remission with improvement and the most recent treatment will be given credit for the cure. It is necessary, therefore, to follow patients under any form of treatment for a long enough time to meet the criticism of natural remission. This has been done. Silbert found that 64.% of Buerger's cases untreated required an amputation within five years of the onset of symptoms. A similar series treated by this method reduced the number of amputations to only 7.6% within the five-year period. The proof of the pudding is in the eating — Buerger's disease is a disease which progresses by interrupted stages to ultimate amputa-

tion in most cases. If, then, the number of amputations can be materially and convincingly reduced, we will have evidence of the efficacy of the form of treatment employed.

Buerger's disease continues, then, to be a disabling condition, the very treatment of which is itself distressing. Toward its ultimate better understanding, however, some progress may be made by the study of bio-chemical forces within the body, whether disturbed or normal.

POSTPARTUM CARE

DOUGLAS E. CANNELL, M.B., B.Sc. (Med.)

Postpartum care is one of the most fruitful fields for advancement of public health. It is, at the same time, one of the more neglected opportunities for good service. Too many physicians either never see their patients following immediate convalescence from delivery, or are content with a cursory history and still more inefficient examination. To illustrate the value of more adequate postpartum care, it is my purpose, briefly, to review the work of a small clinic which has been under my supervision for the past nine months at the Salvation Army Women's Hospital. Prior to its establishment, postpartum cases were not segregated and insufficient time was available to care adequately for them in pre-natal clinics.

Postpartum care entails an adequate history, pelvic examination and treatment of any disorders which may be discovered.

History

Patients are requested to present themselves for examination six weeks following delivery. A careful, but brief, history is taken, in which parity, type of delivery and hospital course are carefully noted. Following a consideration of general health, a more detailed inquiry is conducted to determine the presence of any of the following symptoms: bleeding, vaginal discharge, backache, incontinence (urinary or fecal), bearing-down sensations or pelvic pain. Other complaints which may be volunteered should be noted. Particular care must be taken to see that the patient is aware of the meaning of incontinence. Many fail to elicit this symptom through the patient's misunderstanding.

Pelvic Examination

Pelvic examination is one of the easiest and most useful forms of physical examination, yet its value is constantly jeopardized by lack of systematic consideration and attention to detail. The patient should be placed on an examining table in a good light, with a simple perineal drape. The thighs are abducted, the knees are flexed and the heels approximated or held in stirrups. The vaginal outlet is carefully examined to determine the presence or absence of stigmata of specific infection in Skene's glands, the urethra and Bartholin's glands. The former may be found on careful digital stripping of the urethra, the latter by palpation betwen the thumb and fingers of the examining hand. The condition of the perineum is then noted with and without straining efforts by the patient. A small cystocele or rectocele may be missed if the patient does not strain. At this time descent of the cervix or uterus is noted, if it is present. Proceding further, the position and condition of the cervix are considered. The position, size and mobility of the fundus, together with any other concomitant abnormality are then noted by bimanual examination. Careful alternate palpation of the fornices to determine the condition of the broad ligaments, ovaries and tubes, completes the bimanual examination. A bivalve speculum is inserted gently with the maxi-

mum pressure posteriorly; at its greatest depth, it is opened widely, exposing the cervix, for visual inspection.

Treatment

All patients with evidence of specific infection are referred to Gynaecological clinics for further investigation and treatment.

Perineal relaxations are noted and if marked, the patient is advised to have plastic operations done at a later date. The severity of the lesion, with its associated symptoms, the parity, and possibility of imminent subsequent pregnancies must influence the physician's advice in this respect.

Retroversions are present in about twenty per cent. of all women, the incidence being materially increased in postpartum patients. These displacements are easily diagnosed and readily corrected. The use of the tenaculum on the cervix with downward traction, succeeeded by a sweeping posterior movement will replace most retroversions. This manoeuvre is preceded by gentle efforts with the examining fingers to mobilize and lift the fundus forward.

Following replacement, a fitted, moulded Smith-Hodge pessary is inserted to hold the uterus forward. The rarer, more difficult cases may require massage in the posterior fornix. This is done with the patient in the knee-chest position, the vault being exposed with a Sim's speculum. A pad of cotton with a uterine dressing forcep as a holder, is used to massage the cervix and posterior fornix. This treatment is followed by vaginal packing with tampons. One or two such treatments usually suffice. The uterus comes forward or is replaced with the tenaculum. Follow-up treatments consist of a recheck in one week and four to six visits thereafter at four-week intervals, when the pessary is cleaned and replaced.

Cervical lesions are of the utmost importance. The incidence of carcinoma of the cervix would be materially reduced if all cervices were restored to a healthy state. It is our present practice to cauterize all erosions with the small electric office cautery. Those failing to respond to this therapy require surgical treatment.

Adnexal conditions, such as cellulitis, salpingitis and associated pathology, are treated as the indications arise.

A report of the findings in the above clinic may prove useful in evaluating the importance of postpartum care. These will be considered under the following divisions:

(1) Relaxations. (2) Displacements. (3) Cervical lesions. (4) Other pathological findings.

Relaxations

There were one hundred and seventy-two patients in this series, seventy-two were primiparae, one hundred were multiparae. Relaxations were arbitrarily considered as mild, moderate and severe. The latter term was limited to those of sufficient severity to warrant surgical interference. No primiparae fell in this group, two, on the contrary, had some degree of dyspareunia following perineal repairs at delivery. The vast majority of multiparae showed some degree of relaxation, nine were considered severe, three of these having marked uterine prolapse. Temporary incontinence of urine was observed in six cases, in two of which it was relieved by correcting concomitant retroversions. Consideration of the condition of the perineal floor in primparous patients, with and without episiotomy, proved interesting. There were thirty-four with episiotomy, of which eighteen presented some degree of relaxation, while sixteen out of thirty-eight without episiotomy were considered to be relaxed. This apparent failure of episiotomy is explained on the basis that the majority were medio-lateral in type and the incision was made with the head on the perineum, at a time when damage to the supporting structures had already been done. The mid-line incision is unquestionably better than the medio-lateral type, in this respect. In this series,

there were only two median episiotomies, the results being satisfactory in both instances. An additional discrepancy may have resulted from the fact that many cases without episiotomy had had mid-line lacerations with satisfactory repairs.

Displacements

Fifty-three or almost thirty-one per cent. of patients had retroversions. Thirty-seven were replaced and the great majority of these permanently cured with pessaries. Sixteen were considered failures, but of these only two received treatment. The remaining fourteen either refused replacement or failed to return for further therapy.

Cervical Lesions

Cervicitis was the commonest pathological finding. One hundred and eleven showed some degree of inflammation. In sixty-five, the involved area was less than two centimetres, while in the remaining forty-six, it was two centimetres or more in diameter. Seventy-four were cauterized and to date all of these observed have been cured by this therapy. One required a second treatment. After observing the results following the use of topical applications, douches, etc., it was obvious that cauterization produced the most rapid, permanent and satisfactory healing. Other methods have consequently been discarded in its favour. Complications following this procedure are few, one case bled somewhat excessively, and one developed a mild pelvic cellulitis. Care must be exercised to guard against cases with pelvic infection or recent gonorrheal cervicitis being treated by this method. Instances of severe pelvic infections, initiated by such errors, have been reported.[1]

Other Lesions

A variety of other lesions were observed. These included chemical ulceration of the cervix, six fibromyomata uteri, of which none warranted surgical intervention, and one large ovarian cyst. Two patients with complete tears and satisfactory repairs were observed. Several patients with severe secondary anaemia were treated in the usual fashion. A few whose mental and physical condition warranted sterilization were advised to return for subsequent treatment. A variety of minor medical conditions came under observation, but details of these have no place in this review. This summary of a small group of cases indicates roughly the considerations evident in the care of postpartum patients and the procedures necessarily involved in their treatment.

Conclusions

(1) A summary of the findings in one hundred and seventy-two postpartum patients is submitted for study.

(2) Careful, adequate postpartum observaton, examination and treatment is indicated in all cases.

(3) The satisfactory results obtained in treating puerperal retroversions by replacement and pessaries have been noted.

(4) The excellent results observed following cauterization of the puerperal cervix warrant the adoption of this procedure in all cases.

(5) The comparative consideration of the perineal floor following delivery of primiparous patients with and without episiotomy, suggests that the earlier use of episiotomy and the more frequent adoption of the median type is indicated.

References

(1) Cannell, Douglas E., and Douglass, Marion. — Complications Following Cauterization of the Cervix Uteri, American Journal of Obstetrics and Gynecology, Vol. 30, 376, September, 1935.

ERYTHEMA NODOSUM AND TUBERCULOSIS*

R. M. PRICE, M.B.
From the Laboratories of Pathology and Bacteriology, University of Toronto.

Erythema nodosum is defined as an inflammatory disease of the skin, accompanied by a variable degree of constitutional disturbance, and characterized by an eruption consisting of rounded or oval painful nodules situated on the extremities, which persist for two or three weeks, and then disappear spontaneously. Frequently an attack of erythema nodosum is followed by the development of active tuberculosis in the lymph glands, pleurae, lungs and meninges.

The etiology of this disease still awaits solution. Mackenzie[1] nearly fifty years ago, considered the disease as rheumatic in origin. This view was hardly questioned until 1905, when Lendon[2] advanced the belief that it was a specific fever with an orderly sequence, a period of invasion, infectivity, and a seasonal incidence.

Inasmuch as it had not been definitely established that erythema nodosum had a specific cause, Abt[3] suggested that the condition should be regarded as a manifestation of an infectious disease of unknown etiology, which acts by preparing the soil for the tubercle bacillus.

The reports of scattered cases of this disease, accompanied by streptococcal sore throat, and the discovery by Rosenow[4] of a gram-negative diphtheroid bacillus in the lesion itself, further confused the issue. Hildebrandt,[5] Kober[6] and Judassohn[7] in Germany, and Landouzy[8] and his associates in France, on grounds of clinical and laboratory evidence, incriminated the tubercle bacillus as the etiologic agent in the disease.

Lately the hypothesis that erythema nodosum is intimately associated with tuberculosis has been gaining ground. Ernberg[9] showed the association between erythema nodosum and early tuberculosis of the lung. He and Pollak[10] have shown that a high percentage of patients with erythema nodosum are very sensitive to tuberculin, and that this hypersensitivity tends to appear at at the same time as the erythema nodosum.

The writings of various other authorities tend to confirm the tuberculous nature of the disease. Vetleson[11] found that 26 per cent. of his cases of erythema nodosum had clinical tuberculosis. Wallgren[12] found that 97 per cent. of his series reacted to tuberculin. Massini[13] observed that 14 out of 19 individuals with the rash, had clinical tuberculosis in some form.

Heimbeck[14] reported in a series of 37 pupil nurses with erythema nodosum, 16 developed pulmonary tuberculous, 4 pleurisy, and one pleurisy and peritonitis.

That the tubercle bacillus is the etiological factor in erythema nodosum is supported by Symes[15]. Collis[16] in a comprehensive study of 14 cases of the disease in children, found nine to be definitely associated with tuberculosis, and six with streptococcal infection. He expresses the belief that whereas the tuberculous origin of the disease is proven in some cases, the rheumatic origin is dominant in others.

On this continent, Stokes[17] of the Mayo Clinic, in a study of 10 cases of the disease, found four to be definitely tuberculous, four highly suspicious of tuberculosis, and two which conformed morphologically to the conventional rheumatic type of erythema nodosum, as suspicious of tuberculosis. Foerster[18] reported two cases of the disease in sisters who, following an attack of erythema nodosum, developed tuberculous cervical adenitis. One recovered; the other, four weeks after the onset of the nodosal

*This research was carried on under a grant from the National Research Council of Canada.

rash, developed tuberculous meningitis, to which she succumbed one week later.

Ross,[19] in a study of 60 tuberculous nurses, found four had had erythema nodosum. He expresses the belief that erythema nodosum should be classed with the same relationship to tuberculosis as pleurisy with effusion.

Cruise,[20] in a study of 33 pupil nurses with erythema nodosum, reported that seven developed pulmonary tuberculosis, and four were considered clinically suspicious of the disease

Thus a review of some of the literature on the subject tends to indicate that the association between erythema nodosum and tuberculosis is more than accidental. Although some of the writers are not altogether in accord as to the etiologic significance of their observations, nevertheless, the large and increasing numbers of observations on the association of erythema nodosum with tuberculosis is significant, and deserving of further study.

For the past three years we have interested ourselves in the possible etiologic relationship between erythema nodosum and tuberculosis. A summary of 15 cases of this disease in children revealed the following interesting facts:

1. The onset of the disease was with fever and malaise.
2. The nodular rash appeared three or four days after the onset, and was limited to the lower extremities.
3. The lymph nodes, cervical, inguinal and axillary were frequently involved.
4. The spleen was occasionally palpable.
5. The intracutaneous tuberculin reaction was positive in 14 out of the 15 cases.
6. There was known contact with open pulmonary tuberculosis in six cases.
7. In one case studied, the erythema nodosum in the child led to the discovery of the contact, an open case of pulmonary tuberculosis.
8. The Roentgen examination of the chest revealed in all but one case, opacities in the lung or enlarged tracheo-bronchial glands.
9. In the case where the tuberculin test was negative, and contact with tuberculosis denied, the child was found to have had chorea, suggesting a possible rheumatic origin of the disease.
10. In three of this group, the attack of erythema nodosum was followed by parenchymatous disease in the lung.

Thus, clinically and roentgenologically, there appears to be considerable evidence which would tend to incriminate the tubercle bacillus as the possible etiologic agent, or as an associated factor in the majority of the cases of erythema nodosum in this group.

Inasmuch as it is difficult to obtain material for study from these patients, we decided to attempt to isolate the tubercle bacillus from the circulating blood. In all, we have, up to the present time. obtained blood from nine cases of the disease in children. The procedure which we follow is to obtain blood daily during the febrile stage of the disease. The red cells are laked with sterile distilled water and centrifuged. The sediment is washed with saline, centrifuged and seeded upon our routine and modified culture media used in the cultivation of the tubercle bacillus, and guinea pigs are inoculated. In all instances in this group, we have failed to demonstrate tubercle bacilli culturally or biologically.

Three adult cases of erythema nodosum were also investigated. In two instances, the results were culturally and biologically negative; in the third instance, a young adult, we succeeded in demonstrating the tubercle bacillus in the circulating blood.

CASE HISTORY—E. S., age 16 years, was admitted to St. Michael's Hospital on January 17th, 1933, for confinment of second pregnancy. Normal delivery. Puerperium not remarkable

until the ninth day, when the patient's evening temperature rose to 100°F.; on the thirteenth day postpartum the temperature rose to 103° F. Erythematous nodules made their appearance on legs and arms. Spleen palpable on 23rd day after the onset of fever. Intracutaneous tuberculin test on that day very strongly positive. Physical signs and X-ray evidence of active tuberculosis in the left apex on the 25th day after the onset of the rash. Cavernous signs appeared and persisted until the 60th day. Fever persisted. Left hospital, against advice, after 80 days.

Blood obtained from the patient 23 days after the appearance of the erythematous rash, and just prior to the demonstration of the tuberculous process in the left apex, yielded tubercle bacilli on guinea pig inoculation, which proved of human type on culture.

DISCUSSION—The isolation of the tubercle bacillus from the blood stream of an individual suffering from erythema nodosum, who subsequently developed active tuberculosis of the lung, is significant. It is interesting to speculate that the invasion of the blood stream occurred at the time of the second rise in temperature (13th day postpartum) and coincident with the appearance of the erythematous rash. That the infection was systemic is further apparent from the fact that the patient continued acutely ill with fever, malaise; and the spleen became palpable. The intracutaneous tuberculin test at that time was very strongly positive.

It is further interesting to speculate upon the relationship between the tubercle bacillus invasion of the blood stream and the skin lesions. This individual did have a period of invasion, prior to the appearance of the rash, as manifested by the initial rise in temperature, which was followed by a second rise, coincident with the appearance of the rash. Whether the skin lesions are specific, or whether they are in the nature of an allergic reaction in the skin due to the tuberculo-toxins, or whether they are due to causes unknown, which merely tend to prepare the soil for the tubercle bacillus, we are not prepared to say.

That the erythematous rash was followed by active tuberculosis in the lung, and that there was in the interval a tubercle bacillus bacillaemia, further strengthens the belief in the relationship between erythema nodosum and tuberculosis. We believe that every case of erythema nodosum should be considered and treated as tuberculous, until otherwise proven.

I am indebted to Dr. E. A. Broughton for the use of the clinical data in this case.

References

1. Mackenzie, S.: Clin. Soc. Proc., London, 1886-19-215.
2. Lendon, A. E.: Nodal Fever, London, 1905.
3. Abt, I. A.: J.A.M.A., 1904-63-1454.
4. Rosenow, M. J.: Trans. Amer. Dermat. Assoc., 1914.
5. Hildebrandt: Munch. Med. Wochen., 1907-23-210.
6. Kober, S. B.: Med. Klin., 1912-17-781.
7. Judassohn, L.: Kongr. d. deutch. dermat. Gesselsch., Sept., 1913.
8. Landouzy: Gaz. d. hos., 1913, 34-2098, Press Med., 1913, 941.
9. Ernberg, H.: Jahrb. f. Kinderk, 1921-951.
10. Pollak, R.: Wien. Med. Wochensch., 1921-25-1.
11. Vetleson, G.: Tubercle, 1922-3-433.
12. Wellgren, J.: Jahrb. f. Kinderk, 1927-117 (Third Series).
13. Massini, T.: Schweitz, med. Wochen., 1927-57-708.
14. Heimbeck, J.: Arch. of Int. Med., 1931-22-347.
15. Symes, J. O.: Tubercle, 1930-11-154; Brit. Med. our., 1921-2-741.
16. Collis, A. R. F.: Quart. Jour. of Med. (New Series, 1932-1-141).
17. Stokes, J. H.: Collected Papers of the Mayo Clinic, 1918-10-541.
18. Foerster, O. H.: J.A.M.A., 1914-63-1266.
19. Ross, E. L.: J.C.M.A., 1930-27-347.
20. Cruise, J. F.: J.C.M.A., 1932-27-603.

Thanks are due to Dr. D. E. S. Wishart for his generous help in the preparation of this paper.

PROTAMINE INSULIN

R. B. KERR, B.A., M.D.
Department of Physiology

Since the discovery of insulin, there have been many efforts directed toward its improvement as a therapeutic agent. Attempts to administer insulin by any other route than by subcutaneous injection have largely failed, certainly as far as its clinical use is concerned. It is recognized that small frequent doses of insulin are much more effective than large doses given less often; this is probably due to the fact that some of the insulin is excreted or destroyed when given in large doses. Thus an insulin which is slowly absorbed would be of considerable advantage in the attempt to render the diabetic patient more nearly normal.

These facts have stimulated investigators to attempt to secure such an insulin with the property of slow absorption. The first effort toward this end was that of Burgess, Campbell, Osman, Payne and Poulton,[1] who used insulin in a solution of gum arabic. A definite prolongation was obtained in animals and also in diabetic patients. However, urticarial reactions prevented further work with the latter. Leyton, by adding insulin to various oils, obtained a more prolonged effect. Suramyi and Szala[2] and later, Skouge and Schrumpf,[3] found that a suspension of insulin and lecithin produced a delayed action of the hormone.

The addition of metallic salts to insulin has been carried out by many investigators. Bertrand and Machebeeuf[4] added nickel and cobalt, Maxwell and Bischoff[5] used iron salts. The work of Scott and Fisher[6] of the Connaught Laboratories in which zinc salts were added to insulin is probably the most interesting. It was previously found that zinc appeared to be an important factor in the formation of crystalline insulin. This led to the attempt to add zinc salts in larger amounts to insulin; it was found that this produced a lengthening of the time of action of insulin to a marked degree.

Probably the most promising work leading to improvement of insulin is the introduction of protamine insulin by Hagedorn, Jensen, Krarup and Wodstrum[7-8] of Copenhagen Denmark. Protamines are relatively simple compounds containing many molecules of only two or three amino acids. They seem to be closely related to nuclear tissues and thus have as their most plentiful sources such glands as testicle and thymus. Protamines possess the property of uniting with proteins to form a compound which may be rendered soluble at certain hydrogen ion concentrations and insoluble at others. Hagedorn and his collaborators have taken advantage of this fact by uniting the protamins obtained from the sperm of rainbow trout with insulin, which is itself a protein in all probability, and have obtained a compound which is precipated at the hydrogen ion concentration of the body tissues. This precipitate is used for injection and is found to be much more slowly absorbed than is regular insulin.

Clinical trials in Copenhagen would indicate that protamine insulin will be of considerable benefit to patients suffering from diabetes mellitus. The boon to the patient will be, among other things, the maintenance of a more uniform level of the blood sugar, thus preventing to a large extent the wide variations of blood sugar which are encountered in some individuals when regular insulin is used. There is also the possibility in some patients that the number of doses per day may be reduced. The incidence of hypoglycaemic reactions may become somewhat less. A report confirming the work of Hagedorn has already been published

by Root, White, Marble and Stotz[9] of Boston. Clinical trials are being conducted in local hospitals at the present time.

Scott and Fisher of the Connaught Laboratories have obtained protamine preparations from the sperm of various Pacific salmon. There will be, however, no protamine insulin available for general distribution until the summer or early fall.

Work on normal and depancreatized dogs has demonstrated the prolonged and gradual action of protamine insulin. Depancreatized dogs have been maintained "sugar free" on a liberal diet with only one dose of protamine insulin daily; this is impossible with regular insulin. It has been found possible to give dogs larger doses of protamine insulin than of regular insulin without the occurrence of hypoglycaemic reactions.

While there is much experimental and clinical investigation yet to be done concerning this new form of insulin, there would seem to be little doubt that protamine insulin or some similar compound will soon take an important part in the treatment of many cases of diabetes mellitus.

References:

1. Burgess, Campbell, Osman, Payne and Poulton: Lancet, **205**, 777, 1923.
2. Suramyi and Szalai: Klin. Woch., **9**, 2195, 1930.
3. Skouge and Schrumpf: Zeit. f. Klin. Med., **120**, 754, 1932.
4. Bertrand and Macheboeuf; Comp. rend. Acad. de Sc., **182**, 1504, 1928; **183**, 5, 1926.
5. Maxwell and Bischoff: Am. J. Physiol., **112**, 172, 1935.
6. Scott and Fisher: J. Pharm. and Exp. Ther., **55**, 206, 1935.
7. Hagedorn, Jensen, Krarup and Wodstrup: J.A.M.A., **106**, 177, 1936.
8. Krarup: Clinical Investigations into the action of Protamine Insulinate, Copenhagen, 1935.
9. Root, White, Marble and Stotz: J. A. M. A., **106**, 180, 1936.

CANADIAN LABORATORY SUPPLIES
LIMITED

Canada's Leading Laboratory Supply House.

Headquarters in Canada for
LABORATORY APPARATUS
AND CHEMICAL REAGENTS

MONTREAL, QUE.
296 St. Paul St. West.

TORONTO 2, ONT.
437-439 King Street West

CORAMINE "CIBA"

CIRCULATORY AND RESPIRATORY STIMULANT

Coramine is a 25% solution of pyridine-b-carboxydiethylamide. By a direct influence on the centre, it acts as a most efficient respiratory stimulant; increasing both the depth and the rate of respiration.

Coramine stimulates the heart, leading to an increase in the output of blood; at the same time it tends to cause vascular relaxation, so that, with or without a rise in the blood-pressure, the rate and efficiency of the circulation are improved.

AMPOULES — LIQUID

Ciba Company Limited
MONTREAL

in keeping with the times

Since our laboratories presented Emmenin Collip in 1930 the endocrines have been established as a highly important and growing field for medical endeavour. The marked effect of pituitary substances in a great variety of disorders has been well demonstrated in the mass of clinical data now available, but it is only recently that any of the individual factors of the anterior hypophysis have been successfully prepared. In keeping with the trend of glandular therapy we are now able to offer several of these factors of the anterior hypophysis.

Excepting as otherwise described, sterile solutions of the following anterior hypophyseal factors are prepared and standardized in accordance with the technique of Dr. J. B. Collip, Dept. of Biochemistry, McGill University. All these solutions are prepared for subcutaneous or intramuscular injection.

POLYANSYN

Indications—Conditions such as Simmonds' disease or general hypofunction of the anterior hypophysis; also, post-operatively in some cases following the removal of hypophyseal tumours.

PROLACTIN

(lactogenic factor)

A sterile solution of the lactogenic factor of the anterior hypophysis, prepared in accordance with the technique of Drs. Oscar Riddle and Robert W. Bates (*J. Pharmacol. & Exp. Therapeutics* **55**:*365, 1935*).

Indications—To stimulate lactation in the presence of a developed mammary tree.

MATURITY FACTORS

(gonadotropic)

Indications—Amenorrhoea, sterility, cryptorchidism (undescended testes) and infantilism.

THYREOTROPIC FACTOR

Indications—non-myxoedematous hypothyroidism and myxoedema.

ADRENOTROPIC FACTOR

Indications—Owing to its effect in restoring towards normal the cortex of the atrophic adrenal of the hypophysectomized animal, cases of hypo-adrenalism may be benefited by the trophic influence of this factor, particularly when pituitary hypofunction exists.

AYERST, McKENNA & HARRISON, LIMITED

Biological and Pharmaceutical Chemists

MONTREAL CANADA

DIZZINESS

By R. E. HAIST, '36.

Dizziness is a symptom which all of us have experienced. It is the consciousness of a disturbance in equilibrium ranging from a mere feeling of uncertainty to actual systematized vertigo. Because of this great variety in the type of dizziness, some attempt at classification is required. To this end we shall first divide dizziness into two broad groups: (1) systematized dizziness or vertigo, and (2) non-systematized dizziness.

Systematized Dizziness, or vertigo, has been described in many ways. For the purpose of this paper, we shall define vertigo as the consciousness of a false sense of movement, to which is added an irresistable impulse to make compensatory motor adjustments. Three facts are emphasized by this definition: (1) The conscious element, (2) the sense of definite movement, (3) the realization of the inability to make an adequate motor adjustment. This includes a subjective or objective unsteadiness which persists after the attack and is an essential part of the phenomenon. We may further subdivide systematized dizziness according to the movement sensed. This movement may be (1) of the surrounding objects, (2) of the self, without movement of the surrounding objects, (3) of the self and of the surroundings. This movement may be in any direction and may be rotary or linear in form.

Non-systematized dizziness, or what we may term giddiness, is the sensation of an uncertainty in equilibrium which is vaguely described. It takes in those forms of dizziness not included under vertigo.

Since dizziness requires the consciousness of a discord in the complex of afferent impulses involved in maintaing equilibrium, it is well to consider briefly how equilibration is achieved.

"The knowledge of the body's orientation in space depends on the integration by the nervous system of afferent impulses from a number of sensory receptors, especially from the retinae, the ciliary muscles, the extra-ocular muscles, the semi-circular canals, the otolith organs, the joints and muscles of the cervical spine and the proprioceptors of the lower extremities." The eye, the ear and the kinaesthetic sense endings have central connections with the cerebellum and the cerebral cortex. Through these central connections, the impulses are co-ordinated and activation of the effector system occurs, thus bringing about the appropriate muscular response. Vertigo may result from the loss or disorder of the afferent impulses from any of these receptors or from a disturbance of their co-ordinating mechanism. It is our plan to show where, in this system, local lesions producing dizziness commonly occur and also, how general or remote disturbances can act upon the system to give the sensation of dizziness. We shall, therefore, deal with dizziness arising from disorders of the ear, the eye, and the kinaesthetic sense, with dizziness due to lesions of their central paths, and with dizziness due to general or remote disturbances acting upon the system described *We shall attempt to point out the type of dizziness encountered and, roughly, how the location of the disturbing lesion may be determined in each instance.*

The Ear

First, let us consider the ear and its relation to dizziness. The vestibular apparatus is the sensory receptor of the ear involved in this phenomenon. It consists of the semi-circular canals, the

utricle and the saccule. Dizziness of aural cause is due to direct or indirect involvement of the vestibular apparatus. It may be stimulated physiologically, by turning, swinging, etc., by caloric stimulation, or by galvanic stimulation; pathologically, by a number of conditions we shall deal with presently. Dizziness occasioned by excessive physiological stimulation is accompanied by a definite nystagmus, past pointing, a tendency to fall, and nausea and vomiting if long continued. Pathological involvement of the vestibular labyrinth gives similar associated phenomena. These lesions fall into several groups.

I. Conditions affecting the labyrinth indirectly by way of the stapes and round window:

(a) Violent blow on the ear.
(b) Wax plug in the external meatus.
(c) Ankylosing ossiculitis.
(d) Otosclerosis.
(e) Cholesteatomatous masses in the attic.
(f) Blocked Eustachian tube.

II. Inflammatory processes:

(a) Chronic suppurative otitis media.
(b) Acute non-purulent labyrinthitis.

III. Sudden vascular changes:

(a) Embolism or spasm of the internal auditory artery.
(b) Local haemorrhage.

IV. Conditions giving normal caloric sensibility by exposure of the inner tympanic wall:

(a) Large, dry perforation of membrane.
(b) Radical mastoid operation (occasionally).

V. Conditions giving rise to unilateral change in labyrinthine pressure:

(a) Indriving of the stapes (as in "I." above).
(b) Fistula of the external semicircular canal.
(c) Excess of endolymph by failure of excretion.
(d) Intracellular oedema of the labyrinth.
(e) Alteration in blood volume.
(f) Rise in pressure in the posterior cranial fossa, transmitted by the saccus endolymphaticus.

VI. Toxic influences:

Some causes included in the last two groups will be considered again when we discuss how general conditions may give rise to dizziness.

All the causes we have enumerated produce dizziness by interfering with the harmonic state of the two labyrinths. Dizziness from aural cause is systematized in type, rotary in character and is not relieved by closure of the eyes. It is usually associated with diminished excitability of the semicircular canals, with disturbance of the cochlear functions, deafness and tinnitus, with nystagmus and with a tendency to forced movements. Nausea, vomiting, pallor, and sweating may occur if the attack is severe. Diminished muscle tone is present on one side of the body, and the head is rotated and flexed so that the occiput is directed to the shoulder on the affected side. Systematized rotary dizziness, unaffected by closure of the eyes, plus some of the associated phenomena mentioned, may also be encountered in conditions affecting the intimate central connections of the vestibular apparatus. It should be remembered, too, that general systemic conditions, such as toxaemias, may affect the vestibule or the vestibular nuclei.

As an aid in diagnosing peripheral vestibular conditions, four points are of value:

(1) There is usually some change in cochlear functions.
(2) The dizziness can be altered by the caloric test.
(3) Small doses of quinine cause a diminution of vertigo in unilateral case, if the semicircular canals are at fault.
(4) There is usually proportionate impairment of the response from the "vertical" and "horizontal" canals or of two kinds of reaction from any canal.

Having determined that the vesti-

bular apparatus is involved, we must find out what is affecting it. Most of these conditions previously mentioned as causing vestibular disturbance are obvious on careful examination. If, after a thorough search by history and examination, the cause is not found and yet the dizziness is severe and of the aural type described, we may call it a case of aural vertigo of unknown etiology or we may put it in a class with chronic bronchitis and other symtom-complexes, which have assumed titles they do not warrant and call it Menier's disease.

The Eye

So much for the aural receptor. Now let us consider the eye in its relation to dizziness. The parts of the eye used in spatial orientation are the retinae, the ciliary muscles and the extra-ocular muscles. It should be emphasized that in order to produce dizziness, changes in the eye must be sudden in onset. Ocular dizziness can be produced experimentally or pathologically,

(1) through a sudden distortion of the image or a sudden image difference in either eye obtained experimentally by the use of lenses;

(2) through a sudden failure in accommodation produced by paralysis of the ciliary muscle (e.g., mydriatic);

(3) through a sudden blurring of the image occasioned
  (a) by a muscular imbalance because of ill health or fatigue;
  (b) by astigmatism;

(4) through diplopia or polyopia and false localization produced *experimentally* by means of:
  (a) prisms;
  (b) pressure of the finger on one eyeball,

  Or *pathologically:*
  (a) by a sudden paresis of one of the extrinsic eye muscles;
  (b) by a sudden irregular swelling of the lens as found in incipient cataract.

Mild rotary ocular dizziness may be produced by looking for a long time at moving objects and then looking at stationary objects. Ocular dizziness in which a rotary or linear movement is sensed may occur also with a slight paresis of the extraocular muscles or in a case of late paralysis where restoration of function has begun. *This dizziness is apparent only when looking in the direction of the affected muscle* and may be accompanied by unsteadiness on the feet and by a mild rhythmic nystagmus, more than likely unilateral. The severity and the nystagmus exhibited differs from that of the aural form.

Ocular dizziness is usually mild, non-systematized, and unassociated with nystagmus. The most important single test for ocular dizziness is closing the eyes. All dizziness of ocular origin is relieved by closure of the eye; whereas vestibular and kinaesthetic dizziness is unaffected or intensified. The specific eye lesion causing the dizziness can be determined by history and examination.

The Kinaesthetic Sense

Kinaesthetic dizziness is produced by falsification of sensory impulses from muscles, tendons and joints. Experimental production of kinaesthetic dizziness has not been very successful, because of the wide distribution of deep muscle and joint sensibility. Probably also because of this fact, no lesion of the sensory kinaesthetic receptors is known to give rise to dizziness. All pathological lesions of the kinaesthetic complex considered to cause dizziness are in the afferent nerves or their central connections. Kinaesthetic dizziness is mild, non-systematized, is made worse by closure of the eyes and is always overshadowed by the objective disturbance in equilibrium. The mildness and the fact that lesions in the kinaesthetic paths rather infrequently give rise to dizziness is probably due to the fact that the conditions causing the

interruption are either not very acute or else not extensive enough at the onset, and the patient is permitted to become gradually accommodated to the change.

Lesions of Central Paths

We have seen that dizziness may arise from lesions in the sensory receptors. We come now to dizziness of central origin. This is taken to include all lesions affecting either the afferent nerves previously mentioned or their central connections.

A variety of lesions affect these paths. We shall turn first to conditions affecting the vestibular nerve, the vestibular nuclei, and the cerebellum. Local lesions affecting the vestibular nerve are:

I. Neoplasms lying in the cerebello-pontine angle, including those of the VIII. nerve itself.
II. Aneurysm or aberrant blood vessels.
III. Inflammatory disease.

Vertigo is inconstant and, on the whole, a late symptom of tumours of the cerebello-pontine angle and even of VIII. nerve tumours. In two out of three cases in which the VIII. nerve was divided under local anaesthesia of the superficial tissues only, there was no vertigenous sensation, either when the nerve was being liberated or cut. As a rule, when it does occur, the dizziness occasioned by lesions of the VIII. nerve is not so severe as that of aural cause and is associated with weakness in function of the adjacent VII. and V. nerves. This might suggest that when it does occur, it is not due to involvement of the nerve, but of its immediate central connections.

While lesions of the vestibular nerve may be infrequent causes of dizziness, this complaint is rather often associated with changes in the vestibular nuclei. Conditions affecting the vestibular nuclei and their connections, which may occasion dizziness are:

I. Vascular lesions of the pons and medulla (thrombosis of the posterior inferior cerebellar artery).
II. Inflammatory lesions (encephalitis and syphillis).
III. Degenerative lesions (disseminated sclerosis).
IV. Tumours of the pons and medulla.
V. Vasomotor disturbances in the nuclei.

Posterior inferior cerebellar thrombosis causes a very severe form of systematized dizziness, the intensity and persistence of which may exceed that of labyrinthine origin. It may be differentiated readily from the aural form by the associated signs of analgesia, paraesthesia, hemiataxis and paresis. Rapidly developing lesions in encephalitis and disseminated sclerosis may occasion almost as severe vetigo. These conditions can be diagnosed by the accompanying signs and symptoms. Tumours of the pons and medulla, though involving the structures as the aforementioned lesions, usually give rise to no vertigo—probably because of their slow development. If large enough to give increased intracranial pressure, they may produce a non-systematized type of dizziness. Vasomotor disturbances in the vestibular nuclei are hypothetical rather than proven causes and will be mentioned when we consider the dizziness arising from general or remote conditions.

Examining the vestibular connections further, we find that vertigo is not a common or severe symptom of cerebellar conditions. In acute unilateral lesions, such as those produced by gunshot wounds, dizziness is uncommon except immediately after injury. Vascular or non-suppurative inflammatory lesions are not confined to the cerebellum and hence are of little value as sources of information. Tumours, if confined to the cerebellum and not involving the peduncles, may cause dizziness associated with increased intracranial pressure. Systematized dizziness, due to cerebellar lesions, is usually not found unless the inferior peduncles are involved, when it may be of the most severe form. Cerebellar lesions are associated with other localizing phenomena, such as atonia, ataxia, asynergy,

adiadochokinesia, dysmetria, dysarthria, nystagmus, spontaneous deviation of the eyes, and so on.

Tumours filling the fourth ventricle or arising from its walls may produce paroxysmal or continued dizziness, even without signs of increased intracranial pressure. This is probable due to secondary effects on the vestibular nuclei or the inferior cerebellar peduncles.

Lesions along the ocular and kinaesthetic paths may give rise to a non-systematized type of dizziness, but that they occasion a systematized form or vertigo, is not generally conceded. Lesions in the II., III., IV. and VI. cranial nerves, cause dizziness. This is thought to be due to disturbance of the pupillary and accommodation reflex arc. These paths may be affected by:

I. Inflammatory conditions, such as:
   Neuritis.
   Meningeal exudation at the base of the brain.
   Periostitis.
II. Degenerative lesions, as in Disseminated Sclerosis.
III. Vascular accidents, such as haemorrhage.
IV. Neoplasms.

Central lesions involving the nuclei of the nerves to the eyes may occasion dizziness. For this, the two chief causes are disseminated sclerosis and neoplastic disease. It is said that dizziness may be an early symptom of tumours of the corpora quadrigemina. When dizziness is relieved by closure of the eyes, examination of the II., III., IV and VI. Cranial nerves should aid in localizing the site of the lesion.

Some authors claim that dizziness of kinaesthetic origin may be produced by sudden lesions along the kinaesthetic pathway, such as:

I. Acute Polyneuritis of sensory nerves.
II. Conditions affecting the posterior columns or spino-cerebellar tracts in the cord.
III. Conditions affecting the restiform body.

Information regarding kinaesthetic dizziness is hard to obtain, but it is generally agreed that, where the kinaesthetic path alone is involved, the objective disturbance in the equilibrium overshadows the dizziness and is more permanent.

Since dizziness is a conscious phenomena, the integrity of the cerebral cortex is essential for its appreciation. Whether or not organic lesions affecting the cortex can cause dizziness is a question that is hard to answer. Tumours of the frontal, ocipital and parietal lobes occasion dizziness, but so may supratentorial tumours situated elsewhere. This dizziness is always associated with increased intracranial pressure and hence it is argued that the dizziness is not due to the local damage, but to the pressure increase. Psychogenic dizziness is certainly cortical in origin, but we shall deal with it separately. Other evidence of cortical dizziness is found in the fact that vertigo may occur as an aura in epilepsy. In such cases, the sudden onset, the brief duration and the loss of consciousness which follows, are diagnostic.

Alarming seizures of vertigo, instability, collapse and vomiting may occur with migraine. These seizures are probably due to vascular spasm, but whether of the vessels supplying the vestibule, its central connections or the cortex itself is not known. Signs of aural disease, such as deafness and tinnitus are absent, while a history of previous migraine is obtained.

The dizziness found in patients suffering from the after-effects of head injury is usually non-systematized, being in the nature of a momentary sense of unsteadiness brought on especially by stooping or sudden movement of the head. There will also be impaired concentration, irritability and "nervousness." In a fair number of cases, however, severe vertigo is present. In these, the peripheral vestibular mechanism

functions normally, and, therefore, the damage is thought to be in the central connections.

General or Remote Disturbances

For the purposes of convenience, we have included in our discussion of central dizziness, that due to supratentorial tumor. epilepsy migraine and the after-effects of head injury. We now turn to those conditions which though remote from the equilibrium complex, can affect it by way of the vascular or nervous systems. The number of such conditions is legion. We may group them according to cause under the following heads:

(1) Toxaemias.
(2) Endocrine disorders.
(3) Cardiovascular and Blood changes.
(4) Faulty water metabolism.
(5) Reflex causes.
(6, Increased Intracranial Pressure.

Toxaemia may result (a) from infection, whether focal or general; (b) from abnormal metabolism, or (c) from substances ingested or inhaled. Cases of marked vertigo sometimes clear up when foci of infection are removed. Constipation is a not infrequent cause of mild dizziness. Everybody knows of the vertigenous sensations aroused by a good five-cent cigar and it is said that a "snort" of rum, of gin or of rye has power to alter the motion not only of the individual, but of the world and of the universe at large.

Endocrine disorders producing dizziness are always in the nature of an insufficiency. Some cases of hypothyroidism show marked vertigo while dizzy sensations are often a part of the menopausal picture.

Dizziness is a rather frequent accompaniment of certain cardiovascular changes. With hypertension and arteriosclerosis, the attacks are mild, transitory, and are provoked by changes in posture. Many cases of hyptension give a similar type of dizziness. Sudden severe attacks with nausea and vomiting are seen as part of a vascular accident in the vestibular apparatus or its connections. Aortic regurgitation or congestive cardiac failure may give rise to dizziness by impairing the nutrition of the brain centres or the end-organs. In fact, it may be produced by cerebral anaemia from any cause. The effect of increased intracranial pressure lies either in the cerebral anaemia produced or in a direct action on the equilibratory structures. Hyperactivity of the carotid sinus reflex may give rise to dizziness associated with fainting and convulsions. Leukaemia, by infiltration of the labyrinth or the nuclei, may occasion vertigo General anaemia and polycythaemia are also productive of this phenomenon. The effect of hyperventilation is probably secondary to vasomotor changes occasioned by the reduced CO_2 content of the blood.

According to some, faulty water metabolism causes vertigo. This is by virtue of an interacellular oedema of the labyrinth produced as part of the general process.

We may sum up the discussion regarding the general causes of dizziness by saying *that any process resulting in degeneration, mechanical irritation or disturbed nutrition of the vestibular labyrinth, its nuclei, or of other parts of the afferent equilibrium complex may give rise to dizziness.* It should be remembered that the change must be more or less abrupt in onset and that the type of dizziness occasioned is characteristic of the part of the system affected. But, you may argue, why should anything capable of affecting both labyrinths equally, give rise to dizziness? We must assume either that there exists an asymmetry of vestibular and auditory functions that is unrecognized until these other influences come into play, or else that the effect is on the higher centres themselves.

Psychogenic Dizziness

There is one remaining group of causes to consider. We know that the cerebral cortex can influence many functions of the body. We know, for example, that it may occasion vaso-

motor changes and hence could give rise to dizziness by that means. Also, since dizziness is a sensory phenomenon, hallucinations taking this form can occur. This brings us to the discussion of psychogenic dizziness. The group includes the dizziness that may accompany emotional disturbances in normal individuals as well as that found in the traumatic neuroses and in the psychoneuroses, such as neurasthenia and hysteria.

That disagreeable sights may lead to faintness and dizziness is a matter of common experience. Fear and the related emotions that tend to give a response of withdrawal, are the most frequent emotional causes. In this category, I suppose, comes that dizzy sensation, accompanied by weakness in the knees, a sinking feeling in the abdomen, general mental confusion and a keen desire to be elswhere, which most of the younger ones among us recognize as part of the disorientation associated with an oral "quizz." Fear and the thought of vertigo are sufficient to produce it. Some people possess this ability to a greater extent than others. In the Neurasthenics, it is well marked. They may complain of an almost continuous sensation of unsteadiness. It is generally described as a sensation of the legs giving way and is associated with other neurotic symptoms. Dizziness may be a symptom in hysteria and is especially common in the traumatic neuroses when the head is injured. In the traumatic neuroses the description given may be suggestive of vestibular involvement, but, in nearly all of them, the dizziness disappears on settlement of the litigation.

We have seen not only how varied are the causes of dizziness, but also how they all act by direct or indirect involvement of the *equilibrium complex.* Because of this variety of cause, a thorough history and physical examination should be made in each case. There are several points that I wish to stress, namely: (1) That dizziness is a conscious phenomenon; (2) that psychogenic dizziness is frequent; (3) that ocular dizziness is relieved by closure of the eyes; (4) that aural dizziness shows the same associated phenomena as seen with excessive physiological stimulation of the labyrinth; (5) that systematized rotatory dizziness may be caused by involvement not only of the ear, but also of the vestibular nuclei or of the inferior cerebellar peduncles; (6) that a sudden change of position or movement of the head affects the dizziness if it is due to a vasomotor disturbance or to vascular change.

These are but a few of the points we should remember regarding this very common and always puzzling symptom.

Thanks are due to Dr. D. E. S. Wishart for his generous help in the preparation of this paper.

The J. F. HARTZ CO., Limited

Carry a complete line of

MEDICAL STUDENTS' SUPPLIES

STETHOSCOPES, OTOLARYNGEAL SETS,
HAEMOCYTOMETERS, HAEMOGLOBINOMETERS.
STUDENTS' DISSECTING SETS

32 GRENVILLE STREET TORONTO 5, CANADA

BRONCHIECTASIS IN INFANTS AND CHILDREN

C. H. JAIMET, '36

It is only within relatively recent years that clinicians treating bronchiectasis in adults without much success, began to search for some way or ways to prevent or check this disease at its onset. Intensive study, then, between clinician and pathologist revealed much regarding its etiology—but just as important, too—it showed that a great number of the cases discovered in adults had begun in a very definite way in childhood. This discovery immediately shifted the burden of responsibility to the paediatrician. Since that time rapid advances have been made in all aspects of the disease. I should like to present our present conceptions of Bronchiectasis beginning in infants and children.

Etiology and Pathology

These have been grouped together as I hope to show our present conception of its etiology has a purely pathological basis. The most complicated methods of obtaining sputum for culture have failed to demonstrate one specific organism or group of organisms entirely responsible for its production. Rather it is caused by invasion of those bacteria commonly infecting the entire Respiratory Tract.

Etiologically, then, bronchiectasis is divided into two major groups.

(A) Congenital, (B) Acquired

(A) Congenital. — This group is further divided into: (a) foetal, (b) atelectatic. *The Foetal variety* is rare, and as its name implies is a malformation of the lungs of children who die for the most part in utero. One finds in these lungs, one large cavity or multiple small cystic cavities, which, though they may or may not communicate with a bronchus, are regarded as malformations of the bronchus, rather than of the parenchyma.

The atelectatic type of the congenital variety, as first described by Heller, deserves only a minor part in any classification—since it would seem only a few cases can of a certainty be so labelled. This type arises due to failure of a lung to expand, but (quoting Dr. Warner) there is doubt whether these are abnormal apart from failure to expand, i.e., congenital atelectasis without developmental abnormality. As such, then, perhaps it is safer to include these under the acquired type.

(B) Acquired.—When we come to discuss the etiology of the acquired type, we are confronted with, and confused by, an enormous number of conflicting theories. These have been studied intensively by workers in Toronto, and discarded in favour of one which has now abundant proof in pathological tissue, obtained at the Hospital for Sick Children. Clinicians at this hospital, in an analysis of their cases, were first impressed by the great number of these which suffered from broncho-pneumonia at the onset of bronchiectasis. Of the remaining cases, all except two suffered disease in which bronchitis, or broncho-pneumonia usually occur (i.e., chronic bronchitis, measles, pertussis, influenza, empyema, lung abscess, foreign body). We may go further and say that by far the greatest number of cases have at their onset some form of acute respiratory disease in which the one common thing is acute ulcerative bronchitis. To substantiate such a radical statement, we have Dr. Erb's pathological work on the lungs of more than 13 cases of bronchiectasis. It is pointed out by him, that although all cases do not show the same picture at any given time in the development of the disease, yet there seems to be, pathologically, two main stages in its course.

The First Stage—Destruction

The first of these is the stage of destruction. In six of Dr. Erb's cases, the earliest lesions were not unlike those seen in acute broncho-pneumonia, i.e., bronchioles filled with purulent exudate, some destruction of living epithelium, considerable polymorphonuclear infiltration, yet some of the muscle fibres were intact. The surrounding alveoli were filled with exudate or collapsed. The necrosis of the bronchial wall is not necessarily uniform throughout—a point explaining perhaps fusiform or saccular dilatation. Small fissures were not uncommon, for example, after pneumonia, and when these extended through the bronchial wall, dilatation also resulted. In other cases plugging of the smaller bronchioles with inspissated exudate was outstanding. Yet another case showed a large caseous lymph gland causing central obstruction by pressure, with resultant bronchiectasis.

Six cases have thus been briefly discussed, the duration of all of which was less than six weeks. Yet, while varying degrees of dilatation were seen in all of them, there was *no evidence of epithelial regeneration, or of fibrosis in the parenchyma.*

The Second Stage—Repair

Whereas the process of destruction is measured in days and weeks, repair is measured in months or years. First evidences of repair were noted in only one case before six weeks. The process combined firstly a zone of very vascular granulation tissue in the wall of a bronchus, devoid or nearly so, of muscle and elastic tissue, with superimposed on this tissue at a later date, a relining epithelium of a modified, nonciliated squamous type.

Now, however, we must discuss the relation of pulmonary fibrosis to bronchiectasis for alteration of parenchyma, certainly does occur. In early cases, these were of the nature of acute interstitial pneumonias. Later, proliferation of alveolar and intralaboular connective tissue, led to diminution in size of alveoli and eventually even to extensive pulmonary fibrosis and plural adhesions. Fibrous tissue contracts in any lung, not only at right angles to the bronchi, but also parallel to them. Therefore, the lobe becomes narrower and shorter, the bronchi, wider and shorter, and their mucosa is thrown into transverse folds. This picture is certainly commonly seen in long-standing cases. In answer to the question, does fibrosis precede or follow bronchiectasis, Dr. Erb's seven cases of less than six weeks' duration are again recalled for your consideration. In these, ulcerative lesions of the bronchi were seen, there was destruction of bronchial muscle and elastic tissue, dilatation was present, and yet in none could any pulmonary fibrosis be found, nor any pulmonary adhesions demonstrated. We have now a reasonable and apparently obvious cause for bronchiectasis—acute ulcerative lesions in the bronchial tree. One makes no attempt, however, to say that this lesion causes the full dilation seen in any one, much less every case.

Obstruction certainly plays an important part—and it is through neglect of this factor, rather than consideration of it—that many authors have denied ulcerative bronchitis as the cause. They claim, and rightly so, that if such is the cause, why then, since bronchial infections are so common, is not bronchiectasis more common. The answer I think is inadequate drainage, so that inspissated exudate is allowed to accumulate and obstruct. This in turn favours the progress of septic destruction, or acts as a ball valve during inspiration, i.e., it further increases the difference in pressure during inspiration between the lumen of a bronchus on the one hand, and the parenchyma and pleural space on the other. Since it is an established fact that the bronchial tree psysiologically expands because of this force in health, then in disease an increased pressure on weakened walls which have lost much of their contractibility must of necessity enhance the dilation which now becomes parmanent.

Atelectasis also causes an increased negative pressure, in the pleural space, therefore, congenital atelectasis, and central partial obstruction due to foreign body, new growth, inspissated exudate, lymph glands or aneurysm, are all factors in increasing and maintaining bronchiectasis once a weakening of that wall has occurred by ulceration.

There is one more subject which has merited much discussion. Do upper respiratory conditions, such as tonsilitis, diseased adenoids, repeated nasopharyngitis, sinusitis, etc., lead to bronchiectasis? Or does bronchiectasis cause these? It is a clinical fact in children, that bronchiectasis and one or more of the above conditions are often found in the same patient, and also, striking improvements in the child's condition are noted if these upper respiratory foci are removed. One is inclined to believe that they form a vicious circle. We are well advised to remove such foci, from the standpoint of both preventing the disease and of limiting it.

Signs and Symptoms

Contrary to the reports of Laennec, Graham and a host of other workers who considered bronchiectasis in children to be a very chronic disease unassociated with marked constitutional signs, Dr. Boyd and others in the Hospital for Sick Children state that the general health of most of these patients was more or less seriously affected. The general majority of these presented recurring exacerbation of acute upper respiratory disease. They were considerably below par, re weight, pale and subject to fatigue. When abscesses were present, chronic ill health and profuse foul sputum caused them great incapacitation and inconvenience. Night sweats are complained of frequently, but since fever is often lacking in these cases, they must be due to general ill health rather than to temperature fluctuation. In many cases when cavities were demonstrated, fever was lacking. When exacerbation of acute upper respiratory disease or bronchial pneumonia occur, the fever is that of these diseases. It should be noted that these patients very frequently present themselves to the doctor complaining of symptoms from these superimposed infections rather than the cough sputum or haemoptysis more characteristic of bronchiectasis alone. Cough is one symptom nearly always present in bronchiectasis, though its type and severity varies greatly. In some it is always present, in others it occurs periodically. In most it is affected by posture and when such changes are made, it is productive usually of greater or lesser amounts of sputum. The sputum, like the cough, is usually present. It is foul-smelling in less than 20 per cent. of cases. It is no longer necessary, however, to get a pint a day of sputum, which on standing, settles into the characteristic three layers before bronchiectasis is suspected. It varies in quality, therefore, just as in quantity—it may be scant and tenacious or profuse and pus-like. One quality, however, that it frequently possesses is chunkiness, and this we might well expect from pus produced in cavities through which little air passes. Haemoptysis is more often found in bronchiectasis than in any other pulmonary disease. This I believe is also true in adults. It varies from a slight tinging of the sputum to a sharp haemorrhage. In one case reported, it caused death. Dyspnoea when present (it is entirely lacking in the majority) varies from the mild breathlessness of the run-down child to the almost constant embarrassment in others. Doctor Boyd reports four cases in whom emphysema, upon whose presence severe dyspnoea seems to depend was sufficient to cause a barrel-shaped chest. These children had typical attacks of asthma—but their protein sensitization tests were negative. This symptom, of course, is presented or exaggerated by acute exacerbation of this—or superimposed respiratory disease. Regarding the physical signs in the chest, these are often absent, or very slight indeed. In others, they may be so marked and ex-

tensive that one has difficulty in demonstrating any normal areas over a greater portion of the chest. Perhaps the commonest abnormal finding, is medium crackling rales heard in the lower third of the chest on deep inspiration—produced no doubt by dilated bronchi and an abnormal amount of secretion in these. Pathologically it is found that the parenchyma is frequently—especially early in the disease, very little changed—we would not expect, therefore, to find many signs in such cases. If areas of inflammation and fibrosis or atelectasis are present and if these are extensive enough or superficial enough —then the signs characteristic of these changes are found. The situation of these is of some importance, since the majority of cases of bronchiectasis have pathological tissue present only in the lower lung areas. Though apical bronchiectasis does occur and has been demonstrated in several cases in the Hospital for Sick Children—it is relatively rare—and these must be carefully differentiated from tuberculosis. Shifting of the mediastinum to the affected side is commonly observed and in all of these fibrosis is marked in the parenchyma. The signs in the chest, therefore, will depend on the extent of the lesion, the condition of the surrounding parenchyma, and any superimposed infective process present at the time of examination.

Clubbing of the fingers and toes have also been frequently seen, but these for the most part are present only in those with larger cavities, profuse sputum and of long duration. Evidences of amyloidosis have not been demonstrated in Toronto — but albuminuria of varying degrees is occasionally present. Degenerative changes in the kidney tubules were seen in all fatal cases.

Reference has already been made to the frequency with which upper respiratory infections are present. At least one of diseased tonsils, adenoids, paranasal sinus infection, or nasal-pharyngitis is found in the majority of cases.

X-ray Examination

Although plain X-ray of the chest is usually negative, it may be of aid in ruling out pulmonary tuberculosis, chronic lung abscess or empyema with bronchial fistula. Occasionally, too, dilated bronchi may be seen. If a triangular basal shadow is seen, it is almost surely diagnostic of bronchiectasis — these shadows represent collapsed lower lobes due to obstruction in infected and enlarged bronchi. There are, I believe, only two exceptions to this statement. Such a shadow may be produced by purulent effusion in the pleural cavity —and several cases of congenital heart disease authentically reported have produced a similar shadow. These are so rare as to be disregarded by the ordinary practitioner.

When lipiodal is injected into the bronchial tree and then X-ray examination is carried out, the disease is diagnosed for a certainty. The procedure is most efficiently carried out through a bronchoscope with the child under a general anaesthetic. It is rare indeed for it to be accompanied or followed by any ill effects. When the bronchi present cylindrical, fusiform or sacculated dilatations, the conclusion is obvious. Yet in some cases bronchiectasis is diagnosed without these dilations being seen and this, according to Dr. Warner, brings up an important point to quote— "One of the most important points in the diagnosis of bronchiectasis is the failure of the lipiodol to enter any fine tapering bronchi or to outline normal parenchyma if injected into a bronchiectatic bronchus." Dr. Warner has "never observed a definitely bronchiectatic bronchus which tapered to a very fine bronchiol or where the lipiodol appeared to enter the parenchyma, giving a fluffy appearance." For the errors liable to occur in the interpretation of X-ray films after lipiodol injections, I would refer you to his article.

Diagnosis of Bronchiectasis

In children bronchiectasis must be differentiated from recurring or chronic

bronchitis, lung abscess due to aspiration of foreign body and tuberculosis. In the latter, absence of acid fast bacilli from the sputum may be of help.

The diagnosis can rarely be made on physical signs—the persistent consolidation, moisture or sign of cavitation in the lower lobe certainly suggest it. Bronchoscopic examination will often reveal a foreign body and thus clinch a diagnosis. Chronic bronchitis, it must be admitted, is often impossible to exclude. We have, however, in our lipiodol injection procedure an almost certain method of diagnosis.

Prognosis and Treatment

We have shown, I believe, by the review of pathology—that once a weakened and non-contractible bronchus becomes dilated, its lumen lined by non-ciliated epithelium and its surrounding parenchyma collapsed or fibrosed, we can hope to cure the disease only by removal of these parts—in short, lobectomy, if possible. Similarly, it has been shown that if, after making an early diagnosis, we undertake to remove foci of infection and instigate effective drainage treatment at once, we have at least increased the odds in favoring an arrest of the disease. We base this conclusion on the fact that when infective sputum, mechanical obstruction and other foci are removed, we may arrest the dilation in the bronchi by having thus begun treatment where there is little or no parenchymal collapse or pneumonia. One should like, therefore, to be able to say that, although chronic bronchiectasis can only be cured by absolute collapse or removal, yet early bronchiectasis can be cured or permanently arrested by these means. It is only recently, however, that the disease has been so fully understood, and although two cases in the Hospital for Sick Children have been so arrested in their progress, it is too early to say definitely just what ends will be attained.

As in all disease, prophylactic treatment should be of first consideration. The foci of infection mentioned before should be removed routinely in all children as soon as they are discovered. This method is in practice at the Hospital for Sick Children. Since it unquestionably benefits those with the disease I think we may postulate that it prevents its development in many others. Similarly since bronchiectasis follows measles, whooping cough, pneumonia, etc., in many cases then we should do all in our power to prevent these diseases or at least to give them more careful care during their course. Given a case of bronchiectasis one should remove the cause if it is still acting, e.g., foreign body—these are rare, however. Exacerbations of bronchitis, bronchial pneumonia, etc., should be guarded against by avoidance of infection and by clearing up definite foci where these are present. Fresh air, sunshine and rest do much to make the patient more comfortable. If cough is very troublesome, a mild sedative, such as codeine, may be of some value.

From this point on treatment must be directed toward emptying the cavities and keeping them empty of their secretion. Thus we decrease damage to parenchyma and decrease toxemia. Many forms of therapy have been introduced for this purpose. The most useful are bronchoscopic drainage, postural drainage, collapse therapy, and finally, lobectomy.

Regarding bronchoscopic drainage, early use of this form of drainage not only removes the obstruction in the bronchioles caused by tenacious sputum but it also does it at a time when the ectatic bronchi are still lined with granulation tissue and the parenchyma free of fibrosis. Thus complete cure in many cases is possible.

Postural drainage itself is not sufficient treatment for any one case. In spite of the use of a specially constructed tilted frame to maintain twenty-four-hour drainage during an 8-18 months' period, it was found on a series of cases in the Hospital for Sick Children that relief was given only

while this posture was maintained; as soon as the children resumed their upright position, expectoration began again.

Continuous postural drainage was, therefore, abandoned. Intermittent drainage of ten minutes, four to five times a day is now in use and gives considerable relief, when used, of course, as an adjunct to other types of treatment. For instance, one finds these children can go longer without bronchoscopic suction if they help keep their bronchi open by this postural method.

In these early cases before fibrosis and re-epithelization have occurred, repeated bronchoscopic suction affords the most spectacular results, and if properly carried out over sufficient length of time, cure may be produced. Indeed, it is a possible benefit in all degrees of the disease. In extensive bilateral cases, this, combined with postural drainage, is the only form of therapy that can be practiced. Similarly, too, its early use in lesions high up in the bronchi which cannot be reached by collapsed therapy may prove of great value. In fact, at an early stage in such a lesion it is indeed the only specific treatment we can employ. Finally when lobectomy is to be done, pre-operative treatment by bronchoscopic suction until free of sputum decreases aspiration of septic material at operation.

Artificial Pneumothorax, it would seem, is of value in limiting the disease and should, therefore, be used more often in the acute stages to decrease the dilating forces on the diseased bronchi. It is, of course, itself applicable only to unilateral cases where adhesions are not present. To be of any value, it must be maintained for long periods of time, six months to sixyears. It has the advantage of requiring minimum hospitalization, producing minimum discomfort and gives freedom from symptoms in the majority of cases while maintained. If symptoms recur after expansion, lobectomy must be considered.

Phrenicotomy has many advocates as the form of therapy to be tried when rapid collapse is required, or where adhesions contra-indicate pneumothorax. Its complications—gastro intestinal and diaphragmatic hernia—as well as the insufficient collapse afforded by it in most cases, however, have led to its disuse in the Hospital for Sick Children, except as a preliminary when lobectomy was contemplated.

Lobectomy is rapidly attaining a position in the treatment of this disease similar to that boasted of for thoracoplasty in tuberculosis. That is, in cases past the destructive stage, this form of therapy has given such good results and less radical methods have so often failed that it must no longer be considered as a last resort. Although the mortality is rather high, yet the percentage of absolute cures in cases where life, as long as it lasted, would be a misery, leads us to advocate its earlier use when more conservative measures are contra-indicated, or, when tried, have failed to produce the expected results.

Summary

Bronchiectasis is not due to any specific organism, but is caused, except in those rarer cases of foreign body aspiration, or lymph gland obstruction, to repeated continuous bronchial infection from the bacteria commonly invading the respiratory tract. Pathologists have shown two stages in the progression of bronchiectasis—destruction and repair —the most important features of which are the acute ulcerative lesion in the bronchi, the frequency of mechanical obstruction by exudate in bronchioles, and the absence of fibrosis in the lung during the acute or destructive stage. There are no signs or symptoms absolutely pathognomonic of bronchiectasis. The picture varies with the individual, with the stage of the disease and with exacerbations of acute infection. Chronic cough with chunky sputum after an attack of pertussis or measles make us most suspicious of its presence, and haemoptysis is an important sign. Diagnosis is only made for a certainty by

X-ray after bronchoscopic injection of lipiodol. Prophylactic treatment is ideal, the aims of which are to prevent the disease by clearing up foci of infection in the upper respiratory tract, and, secondly, to prevent permanent dilatation by early instigation of postural drainage and bronchoscopic suction. When the dilatation is established, repeated postural drainage with bronchoscopic suction do most toward alleviating toxic symptoms and decreasing sputum. Phrenicotomy and pneumothorax are of value in arresting the disease in many cases—but after the above have been given a fair chance, lobectomy should be earlier considered, as it is the surest way of establishing a permanent cure.

HORMONES OF THE ANTERIOR PITUITARY

PART I. GROWTH AND SEX HORMONES

R. M. TAYLOR, '39

Experimental work continues to emphasize the importance of the pituitary among the endocrine glands. It has been referred to as the general headquarters of the endocrine system and its designation, as such, seems to be most apt. This article has been divided into a discussion of (1) the growth hormones, (2) the sex hormones, (3) other endocrinotropic hormones, (4) metabolic effects.

The anterior lobe developes from the ectoderm of the stomodeum in the embryo. It grows up as a diverticulum to join an outgrowth from the anterior floor of the diencephalon which becomes the posterior lobe.

The anterior lobe is formed of groups and columns of epithelial cells supported in a reticular connective tissue. Some of the epithelial cells are chromophobe and the rest are chromophil. Among the chromophil cells are alpha and beta, or acidophil and basophil types. The granules in these cells are believed to contain the precursors of the secretion. The chromophobe cells have little cytoplasm and may be old chromophil cells.

During pregnancy the increase in size of the anterior lobe is due to an increase of chromophobe cells. After castration the beta cells increase while the alpha cells decrease. Administration of an anterior lobe extract, thyroid, or epinephrin increases alpha cells. Iodides decrease both alpha and beta cells.

The Growth Hormone.

The earliest description of a hypophyseal disorder was that of acromegaly, by Marie. Its identification with pituitary overactivity was reported by Minkowski. Paultauf later made reference to the reverse condition, dwarfism, due to underactivity of the hypophysis. These deductions based essentially on a hypertrophied or diminished pituitary gland were far from demonstrating the existence in the gland of a specific substance necessary for growth in the higher animals.

A great step forward was the production of dwarfism as the result of extirpation of the gland in young animals. Aschier was the first to demonstrate this and was followed by a host of other workers.

It has been fairly definitely shown in the case of rats that if the operation is performed on animals four weeks old no increase of weight follows even on the best of diets. Care must be taken, however, to avoid injury to the hypothalamus during the operation as such an injury will result in adiposity and a resultant gain in weight. Collip claims that in rats only three weeks old a gain of twenty to thirty grams may occur after complete removal of the anterior pituitary.

If this were the only evidence it would be possible that the dwarfism was a secondary effect due to a metabolic upset consequent on loss of the gland rather than the elimination of a specifically needed substance. But gigantism has been produced in normal female rats (which are more sensitive to the extract than other animals) by the daily parenteral administration of extracts of the anterior pituitaries of beeves. Control untreated rats reached a growth plateau at normal adult stage. The giants were not fat but symmetrically proportioned.

When the maximum response is reached by dosage at any one level of a particular preparation, multiplying the dose shows not the slightest effect in increased growth. The limit of the body's capacity for growth has been reached and hence the limit of the capacity to utilize the hormone. At no time has a rate of growth in excess of the rapid rate for post natal life, been evoked by the growth hormone, nor does a rapid rate continue indefinitely under medication. In from fourteen to eighteen months slowing is evident and one can become convinced that forces other than epiphyseal closure operate to limit growth.

After cessation of treatment of animals there is an abrupt fall in weight which, however, does not affect the skeleton and which may have something to do with water balance.

Even in adult life the hormone seems to be necessary, as it is isolated in large amounts in adult cattle, but why it is necessary is not known as the continuous production of red blood cells and replacement of epithelium is apparently unaffected by hypophysectomy. The distortion of growth in adult life that produces the disease acromegaly has been explained to be the result of growth imposed on the skull and extremeties when stature changes are impossible because of epiphyseal closure. The rat, whose epiphyses do not close until long after sexual maturity, might be expected to show signs of acromegaly if the epiphyses could be made to close earlier.

At present the need is for a specific biology test for the hormone which can be rapidly performed. So far the increase of weight in rats following injection of extract has been used but there is some evidence that the decrease of the glutathione content of the liver following injection can be used as a criterion.

It is not yet clearly established that subnormality of the hypophysis can occur as regards the production of only one of the hormones, for example, the growth hormone, although the prevalent impression is that uncomplicated dwarfism is frequent. Smith has shown that when the thyroid is removed an improved growth of hypophysectomised animals will take place when thyroid administration accompanies that of growth hormone.

As yet replacement therapy with growth hormone preparations after hypophysectomy has not been conducted with pure hormones but growth hormones contaminated with traces of other hormones has restored the stature in animals experimented on by Reichert. It is desirable that growth hormone preparations be free from gonadotropic effects, for it is possible that function of the reproductive system hastens closure of the epiphyseal discs.

As to the mechanism of action of the growth hormone it is possible that it acts directly on the tissues or indirectly through stimulation of other endocrines particularly the thymus. The action on metabolism is just beginning to be analysed. It is shown that urinary nitrogen falls after the administration due to decreased urea excretion. This is no doubt due to nitrogen storage in the tissue as the blood nitrogen falls at the same time. There is a lowering of the respiratory quotient indicating an increased fat utilisation.

The hormone exhibits characteristics of proteins. For extraction dilute aqueous alkali is used and the extracts contain other active substances. It is precipitated by complete protein precipitants but it is not certain yet that

the hormone is not adsorbed on the precipitated protein.

With isoelectric precipitation, although growth hormone goes down with the precipitate, much remains in the supernatant fluid and with re-precipitation less hormone is taken down. The hormone can then be adsorbed on tricalcium phosphate in ammoniacal solution. This substance is free from contamination except by interrenotropic principle.

Sex Hormones.

(a) **Gonadotropic hormones.**—Over twenty years ago Cushing and his coworkers demonstrated that hypophysectomy caused an atrophy of the reproductive system. In 1922 Evans and Long secured excessive luteinization of the ovaries in normal rats by the injection of anterior lobe extracts. In 1927 restoration of gonadal function after hypophysectomy with hypophyseal implants and induction of precocious sexual maturity with the same treatment conclusively demonstrated that the anterior lobe maintained and controlled the activity of the ovaries and testes and through them influenced the other reproductive organs.

Although the extracts thus far prepared do not have the desired physiologic purity, evidence gained from their use indicate that two types of preparation can be made. One of these, in terms of the response in female rate, gives follicular stimulation and the other fraction, the purification of which has not progressed as far as the purification of the follicle stimulator, gives luteinization. As regards the sexes, the former stimulates the germ cell line (male germ cells, ova and granulosa) and is therefore gametokinetic or gametogenic. The latter, the luteinizer, appears to act predominantly on the connective tissue derivatives (the theca cells of the ovaries and the interstitial cells of the testis).

In addition to the fractionation of the hypophyseal gonad-stimulating hormones, gonadotropic substances have been discovered in human blood and urine during pregnancy, after ovariectomy and the menopause in certain tumours of the reproductive organs and in smaller amounts in the blood and urine of men and women during the normal reproductive period. A gonadotropic substance is present in large amounts in the blood serum of mares during approximately the middle third of pregnancy. Certain of these substances seem to come from the anterior lobe but others have a rather uncertain origin.

Work on fractionation of the gonad-stimulating fraction of the anterior lobe has been carried on for a number of years until a fraction has been obtained which in female hypophysectomised rats, in young rabbits or, with limited treatment, in immature rats gives pure follicle growth. In the latter form corpus luteum formation will take place after several days treatment due no doubt to the secretion of the animals own pituitary gland. The effects of injection of follicle stimulating fraction in hypophysectomized females are identical with those secured by injection of the extracts of the urine of post menopause or oviariectomized women. Thus the principle is castrate or menopause urine seems to be identical with the follicle stimulating fraction of the pituitary.

The action of castrate-urine follicle stimulating principle in hypophysectomized males is to cause the seminiferous epithelium of the atrophied testes to show a profound response accompanied by little or no response of the interstitial tissue. The same results are obtained by Evans and Simpson by administration of a fractional extract of the hypophysis.

The present status of a luteinizing gonadotropic hormone is not as definite as that of the gametokinetic fraction. Some workers have reported a fraction from the anterior lobe which when injected alone causes little or no increase in ovarian weight and produces no luteinization unless large follicles are present. If injected with a follicle fraction the follicles that have been

stimulated to growth by the latter then become luteinized. In many respects the gonadotropic principle in human pregnancy urine meets the requirements postulated for a luteinizing principle. Extracts of this urine cause no follicle growth in hypophysectomized rats but produce a luteoid change of the theca cells of the follicle and ac cording to Leonard and Smith true corpus luteum formation of follicles of a size sufficient to be acted on are present. In males either normal or hypophysectomized it produces an extensive interstitial hypertrophy. However, it also definitely stimulates the seminiferous epithelium although this has been denied by Collip. This action may be due to a gametokinetic fraction in pregnancy urine whose action is masked in hypophysectomized females by the luteinizing fraction.

From experiments recently performed it seems that ovulation depends on the concurrent action of the two fractions at a correct stage of follicular development.

(b) **Lactogenic hormone.**—In 1932 Riddle and co-workers isolated the lactogenic factor in a form sufficiently pure to prove its distinctness from growth, gonadotropic and thyreotropic factors.

There is no evidence that the development of mammary tissue is assisted by the lactogenic factor. Some reports indicate that an unidentified pituitary extract favours mammary growth but the lactogenic factor apparently acts on fully prepared mammary tissue solely to initiate and excite milk secretion. Why it is released and the reason for its impotence during pregnancy are unknown but workers at Chicago have advanced the theory that the lactogenic factor is suppressed during pregnancy by oestrogenic substances normally produced in large amounts during this period. At the same time the oestrogenic factor causes growth of the mammary glands. At partrition with loss of the placenta the oestrogenic level in blood drops suddenly and the lactogenis factor in blood is no longer inhibited.

For preparation it must be extracted in acid or alkaline solution, precipitated isoelectrically in water and the precipitate must be repeatedly washed. As thus prepared it contains an inert protein. Salt free preparations at ph8 withstand boiling for an hour with little loss of potency. For assay, the crop gland response in doves or pigeons is used.

PART II.—ENDOCRINOTROPIC AND METABOLIC HORMONES

D. H. COPP, '39

A. Endocrinotropic Hormones

Recent experiments of the past decade have increasingly revealed the dominant position of the anterior lobe of the pituitary in endocrine physiology, controlling the other glands through its endocrinotropic secretions.

We have already considered two of these: The gonadotropic hormones—

1. Prolan A., the gametogenic factor, and
2. Prolan B., the stimulant of the interstitial tissue.

3. **Thyrotropic Hormone** — Aside from the sex hormones, this was the first endocrine control hormone to be investigated. As early as 1889, Rogowitch observed enlargement of the pituitary on thyrodectomy. Then, in 1922, P. Smith, working on hypophysectomized rats, demonstrated marked atrophy of the thyroid after the pituitary was removed. This was confirmed clinically by Graubner, in cases of Simmond's Disease (pituitary atrophy).

Workers now searched for effects of anterior lobe extracts on the thyroid. Loeb and Aron, in 1929, noticed striking hyperplasia of the thyroids of guinea pigs when anterior lobe extracts were injected. This work was conconfirmed by numerous investigators. Eitel, Krebe and Loeser even claim to

have obtained thyroid hyperplasia with thyrotropic hormone in vitro.

The Thyrotropic Principle, obtained first by Collip, is heat labile, inactive when taken orally, and apparently protein in nature. It is distinct from the growth hormone, for it will not produce growth in young recently hypophysectomized rats.

The physiological effects of the hormone have been carefully studied. It is found that injections of suitable amounts over a few days results in hyperplasia of the thyroid, and attendant hyperthyroidism—with increased metabolic rate, heart rate, and exophthalmos. Verzar and Wahl showed that these effects are not present when the thyroid is removed. Apparently its action is due entirely to stimulation of the thyroid.

On hypophysectomized animals, the effects are even more striking. After the pituitary is removed, the thyroid shows signs of involution, and the B.M.R. falls to 75% normal. These animals are extremely sensitive to the thyrotropic hormone, and injections as low as 1-16 the minimal dose producing effects in normal rats will bring the metabolic rate back to normal. This may be the normal maintenance requirement.

If injections are carried over a long period, interesting results are obtained. Injections of thyrotropic principle at first stimulate the thyroid, but as injections are continued, there is a reversal of effect, with decrease in size of the thyroid and of the metabolic rate. Collip, working on guinea pigs, showed that after daily injections for 37 days, the metabolic rate had fallen to the level of hypophysectomized animals. These animals appear resistant, not only to the injected thyrotropic principle, but to that of their own pituitary.

It was also found that injections of serum of these resistant animals into normal or hypophysectomized rats produced in them a corresponding immunity. Scowen and Spence developed resistant serum in a rabbit, and found that when it was injected simultaneously with doses of the hormone, there was no hyperplasia of the thyroid.

Much conjecture has been raised as to the nature of this so-called "anti-hormone." Collip showed that it did not originate in the pituitary, since resistance could be developed just as well in animals when this gland had been removed. He observed hypertrophy of the adrenal cortex in resistant animals, but it has been established that cortin is not the agent.

Thus it appears that the anterior lobe secretes a thyrotropic hormone necessary for normal maintenance of the thyroid gland, injection of which produces thyroid hyperplasia and thus hyperthyroidism. Prolonged injection, however, results in development of a resistant substance in the serum which inhibits the hormone.

4. **Parathyrotropic Hormone** — Recent clinical work has indicated a relationship between tumours of the pituitary and parathyroids. Hertz and Albright, 1934, demonstrated a substance in the urine of patients with parathyroid tumours which would produce in rabbits a hyperplasia of the parathyroids. Smith, 1927, and Houssay, 1933, observed atrophy and degeneration of the parathyroids of hypophysectomized animals. Strangely enough, if the pancreas is also removed, degeneration is very marked, and the blood calcium falls.

Hertz and Kranes, by acid extraction of the anterior lobe, obtained a fraction which they claim stimulated growth of the parathyroids. At the same time, Hoffman and Anselmino noticed an increase in blood calcium when this parathyrotropic principle was administered, but only when the glands themselves were present.

This scanty evidence indicates that there may be a parathyrotropic hormone, stimulating growth and activity of these glands, and through them raising the blood calcium.

5. **Interrenotropic Hormone** — The first indication of the relation of the anterior lobe to the adrenal cortex was

obtained by P. E. Smith in 1930, when he showed atrophy of the cortex in a hypophysectomized rat. Evans confirmed this, and claimed cortical repair on administering anterior lobe extracts. A fraction has been prepared which is said to contain the Interrenotropic Principle. This produces cortical repair in hypophysectomized animals and sometimes even hyperplasia. It is also interesting to note that two cases of Addison's Disease have been greatly relieved by injections of this fraction.

The above evidence, although not conclusive, indicates a hormone elaborated by the anterior lobe, which stimulates the adrenal cortex. As yet, there is little evidence of a hormone controlling the medulla, which seems most intimately connected to the autonomic nervous system.

6. **Insular Pancreatropic Hormone**— Here again, atrophy of the pancreas islet tissue was observed in hypophysectomized dogs by Koster in 1930. Hoffman, 1933, after injections of what he termed a pancreatropic hormone fraction of anterior lobe extract, claims to have obtained increase in size and number of the islets of Langerhans with a slight decrease in blood sugar, due to increased insulin secretion. Paradoxically, in rats there was depletion of liver glycogen, caused perhaps by thyroid stimulation from thyrotropic contaminant, and resulting sugar mobilization.

There may be an anterior lobe hormone controlling normal maintenance of the pancreatic islets, but the evidence is too meagre and conflicting to draw definite conclusions.

B. Metabolic Hormones

The anterior lobe influences metabolism directly—by specific metabolic hormones, and indirectly — by endocrinotropic stimulation of other glands.

The Thyrotropic factor, through the thyroid, increases the B.M.R., and profoundly influences iodine metabolism.

The Parathyrotropic factor similarly produces indirectly a rise in blood calcium.

Some connection with potassium balance has been claimed for the interrenotropic factor, while a pancreatropic principle, if secreted, would have an indirect effect on carbohydrate metabolism.

1. **Diabetogenic** — The first suggestion of such a hormone was the observation by Borchardt (1908) of glycosuria and a diabetic tendency in acromegalic cases. Since 1927, numerous workers have produced hyperglycaemia and glycosuria by injections of anterior lobe extracts.

Houssay in 1932 began some very significant experiments. On removing the pituitary of previously depancreatized dogs, he observed striking relief of the diabetic symptoms. This "Houssay dog" — completely depancreatized and hypophysectomized — is very sensitive to both insulin and the diabetogenic factor. Injections of even small doses of insulin in these dogs produces great hypoglycaemia, and even fatal convulsions. On the other hand, administration of the diabetogenic factor caused hyperglycaemia, glycosuria and acidosis. However, if both are administered simultaneously, the animals react like insulin maintained depancreatized dogs, and the much less sensitive to additional doses of either given at the same time. The two seem to act like a buffer pair, regulating blood sugar.

Much has been learned from a study of hypophysectomized animals. Blood sugar remains normal, except in starvation, when hypoglycaemia develops. Sensitivity to insulin is also greatly increased. Houssay (1933) found the R.Q. normal in toads without a pituitary, and Gaebler confirmed these results in dogs. However, in depancreatized dogs, Houssay found that when the pituitary was removed, administration of glucose then produced a rise in R.Q. This suggests that the anterior lobe acts not only as an anti-insulin agent, but inhibits glucose utilization directly.

This Diabetogenic factor, according to Houssay's work, is soluble in water

and 60% alcohol insoluble in fat solvents, probably protein in nature, and not ultra-filtrable. It must not be confused with posterior lobe extracts, which somewhat resemble it in action. Absent from the posterior lobe, it is found in the anterior lobe extracts associated with the Growth Hormone. It also is present in large amounts in the urine of diabetics. It acts to raise the blood sugar, particularly after insulin injections, when it decreases the hypoglycaemia, and increases insulin resistance.

Clinical evidence substantiates this work. Lucke (1932) found high fasting blood sugar in acromegalics, and low blood sugar with increased insulin sensitivity in a hypopituitary dwarf. The latter's blood sugar was raised by the diabetogenic hormone when injected.

There is much uncertainty as to its mode of action. Lucke believes it acts directly on the nerve centres for carbohydrate metabolism, and claims that injection of the hormone into the spinal fluid produces instantaneous effects. When injected into the blood, Houssay noticed a considerable latent period before the blood sugar rose.

Thus it appears that the anterior lobe secretes a hormone that tends to raise the blood sugar level, acts as an anti-insulin factor, decreases insulin sensitivity, and may inhibit carbohydrate metabolism directly.

2. **Ketogenic Hormone**—Burn and Ling, in 1928, found that they could greatly increase the ketonuria of rats on a butter diet by injections of alkaline anterior lobe extracts. A purified preparation by Magistris of the ketogenic factor was found to have chemical properties similar to the diabetogenic factor, except that it was ultrafiltrable and dialyzable. It was associated with the thyrotropic hormone. A unit has been standardized as the amount which will double the acetone bodies of the blood of a male rabbit in two hours. Injection of this substance results in a sharp rise in acetone bodies of the blood and ketonuria. Magistris claims that it also increases the liver glycogen.

It would appear that the diabetic effect of anterior lobe extracts is due to the combined action of these two hormones, one raising the blood sugar, the other producing ketosis.

With respect to protein metabolism, Houssay found a decrease in glucose and nitrogen excretion of phlorhizinized dogs when the pituitary was removed and from this considers that the pituitary facilitates glucose formation from proteins.

Anti-Hormones

In conclusion, a word should be said of the so-called "anti-hormones" peculiarly associated with many of the anterior lobe hormones. It was found that on prolonged continuous treatment with the latter, the effects fell to zero, or were even reversed. This has been observed with the thyrotropic, parathyrotropic, growth, and ketogenic hormones.

Such developed immunity is not found on injection of other hormones as adrenalin, thyroxin and insulin. Collip has suggested a theory of anti-hormone secretion to explain this, and considers that this may be responsible for many hypofunctional states. Loeb, however, pointing out that the extracts are not protein free, and are all obtained from the same animal, the ox, suggests that there may be a hormone-protein linkage, and formation of antibodies in the immune serum. When crystalline hormones are prepared, it will be possible to test this. At present the explanation is still uncertain.

This necessarily sketchy outline of the anterior pituitary hormones indicates the dominant position it occupies as master gland of the body. Through the diversified hormones, it exercises control over growth, the sex cycle, lactation, the other endocrines and many metabolic processes.

CONSTITUTION
OF THE
UNIVERSITY OF TORONTO MEDICAL JOURNAL

The Constitution of this Journal, which is to be found in Article XIX. of the Constitution of the Medical Society, has recently undergone a complete revision. The revised version of this Constitution appears below. The principal changes that have been made are:

1. A reduction in the number of issues from 7 to 6 per year.

2. Reduction of the subscription fee from $1.25 to $1.00, and inclusion of the subscription in the Medical Society fee, so that every undergrauate in the Faculty will receive the Journal.

3. Extensive revision of the remuneration paid members.

This revision of the Constitution was voted upon at the Annual Medical Elections on February 28th. That the proposed changes have the hearty support of the undergraduates was shown by the vote of 522 for and 128 against the revision.

ARTICLE XIX.—MEDICAL JOURNAL

1.—Name

The name of this publication shall be "The University of Toronto Medical Journal."

2.—Objects

The object of this Journal shall be the publication of scientific papers of prime interest to medical students. It shall also act as the official organ of the Medical Society in reporting student activities. Material shall be contributed, preferably, by undergraduates, graduates, or members of the staff, of the Faculty of Medicine of the University of Toronto.

3.—Management

1. The Journal shall be published six times a year, at monthly intervals, beginning with November 1st.

2. The Editorial Board, as hereinafter defined, shall be responsible to the Medical Society Executive for the publication of the Journal on schedule time, and for the contents of each issue.

3. The Editorial Board shall consist of the following students in the Faculty of Medicine:

a. An Editor-in-Chief, who shall be appointed as set forth in Article XVI., Section (d).

b. An Associate Editor, who shall be appointed as set forth in Article XVI., Section (e).

c. A Managing Editor, who shall be appointed as set forth in Article XVI., Section (f).

4. The Editorial Board shall be responsible for the organization of the Editorial Staff as hereinafter stipulated, for the assembly of material for each issue, and for the proof reading of the same. They shall also be responsible for the organization of the Circulation Staff. At the close of their term of office, they shall nominate the Editorial Board for the ensuing year, such nominations to be handed to the President of the Medical Society.

5. The Editorial Staff shall consist of the Editorial Board and the following additional members appointed by the Board.

a. A Feature Editor from the 6th year.

b. A Women's Editor from the 6th year.

c. Three Assistant Editors, one from 5th year, one from 4th year and one from 4th year of the Biological and Medical Sciences Course.

It shall be the duty of the Editorial Staff to carry out any work allotted by the Editor-in-Chief.

6. The Circulation Staff shall consist of a Circulation Manager from any year, and representatives in each of the other years. The Circulation Manager shall be appointed by the Editorial Board and he shall appoint the year representatives. The Circulation Manager shall be entirely responsible for the distribution of the Journal to Undergraduates, and for the mailing of copies to graduate subscribers, advertisers and contributors.

7. The Managing Editor shall, with the approval of the Editorial Board, let the contract for the printing of the Journal. He shall control the sale of advertising space in the Journal at rates set by the Editorial Board. He shall be entirely responsible for the preparation of advertising copy, and for the collection of advertising accounts.

8. Any form of circularization, or advertising, in the name of the Journal, calculated to draw subscriptions or advertising, must have the approval of the Medical Society Executive before it is used.

9. At the discretion of the Editorial Board, an Advisory Staff shall be appointed from the teaching staff of the Faculty of Medicine. It is suggested that one younger staff member be appointed from each of the major teaching departments.

10. A general meeting of the entire staff shall be held at least twice a year.

4.—Finances

1. The annual subscription rate, for undergraduates, shall be one dollar ($1) payable to the Bursar of the University of Toronto as a part of the Medical Society Fee. This fee shall be in addition to the the present Medical Society Fee and shall be paid by every person who pays the Medical Society Fee. The annual subscription rate for all other subscribers shall be one dollar and fifty cents.

2. All funds payable to the Journal shall be deposited, in a bank, under the name of the University of Toronto Medical Journal, by the Managing Editor.

3. The Managing Editor shall act as Treasurer and pay all accounts by cheque when so ordered by a motion passed at a regular meeting of the Editorial Board, and not otherwise. All cheques shall be countersigned by the Editor-in-Chief.

4. Every member of the Staff (Editorial, Circulation and Advisory) shall, as a reward for his services, receive a free ticket to the Annual Medical "At Home." These tickets, with the exception of the one for the Editor-in-Chief, shall be paid for by the Journal. The following additional remuneration shall be given:

a. The Editor-in-Chief shall receive an honorarium of $35 (Thirty-five dollars).

b. The Associate Editor shall receive an honorarium of $10 (Ten dollars).

c. The Women's Editor and the Feature Editor shall each receive honoraria of $5 (Five dollars).

d. The Managing Editor shall receive the following commission on the gross income from advertising:

10% on the first $200.

20% on the next $300.

25% on any amount over $500.

e. The Circulation Manager shall receive an honorarium of $15 (Fifteen dollars). He shall also receive a commission of 25% of the gross income from all subscriptions other than undergraduate subscriptions.

5. If the Executive of the Medical Society feel that any member of the Editorial Board has failed to satisfactorily discharge the duties of his office, they may order the payment of the whole, or part, of his honorarium (excepting commissions) to be withheld. The Editorial Board shall have similar power concerning the remuneration of the other members of the staff.

6. Complimentary subscriptions to the Journal, for the current year, shall be given to each member of the advisory staff.

7. Two complimentary copies of the current number shall be given to each contributor and advertiser. These copies shall be mailed by the Circulation Manager within 10 days after the publication of each issue.

8. The Managing Editor shall present an up-to-date financial statement to the Medical Society Executive each trimester. A final financial statement, accompanied by vouchers for all money spent, shall be given to the Medical Society Executive before April 30th of each year.

9. Any balance accruing from the operation of the Journal shall be carried forward for the improvement of the Journal in the following year, provided that any deficit incurred by the Journal in previous years has been reimbursed to the Medical Society.

10. The Medical Society shall be responsible for debts and liabilities incurred by the Journal only if the staff follows the constitution as herein set forth.

11. The Editorial Board shall be responsible to the Medical Society Executive for the publication, contents and financial outcome of the Journal. Failure of any one of them to comply with the regulations set forth in any section of Article XIX shall render them liable to dismissal by the Executive.

It is a pleasure to acknowledge the assistance of Dean Fitzgerald and Prof. Linell; of Mr. McInnis, Mr. Scott and Miss Munroe from the Medical Society; and of various members of the staff of the Journal, in the preparation of the revised Constitution.

O. M. S.

ABSTRACTS FROM CURRENT LITERATURE

It is hoped that the present group of abstracts will direct the attention of students to the Bulletin of the Academy of Medicine of Toronto. This excellent journal does not receive nearly as much attention from the students as it merits. Not only does it contain much local medical news of interest to students, but it also presents many papers of great practical value.

Principles of Treatment of Acute Infections of Soft Tissues, Boils, Carbuncles, Cellulitis, and Lymphangitis.

W. G. Carscadden. Bulletin of the Academy of Medicine of Toronto, 1936, **9**, 111.

The pathology and bacteriology of these common infections are discussed and made the basis for an outline of the treatment which is followed in such cases at St. Michael's Hospital. Incision should be deferred until there is definite localization of pus and should then be done in such a way as to avoid bleeding. Magnesium sulphate paste (in glycerin) is recommended as a local application. The uses of vaccines, and staphylococcus toxoid and antitoxin is discussed. Three exceptions are made to the rule that a cellulitis should not be incised till fluctuation is present. The exceptions are infections of the anterior closed space of a finger, acute suppurative tenosynovitis and deep palmar abscess. O.M.S.

Acute Infective Lesions of Joints.—Suppurative.

R. I. Harris. Bull. Acad. Med. Toronto. 1936, **9**, 118.

Organisms may be introduced directly into a joint through a wound, may spread from surrounding tissues or may reach the joint by way of the blood stream. The commonest infecting organisms are staphylococci, streptococci and gonococci. In adults the gonococcus is particularly important. The important pathological change is destruction of joint cartilage since it is the extent of this destruction that determines the amount of function which the affected joint will retain. Suppurative arthritis has, most frequently, to be differentiated from inflammatory rheumatism and osteomyelitis. Since cartilage destruction is largely due to the action of enzymes derived from the leucocytes in the pus early drainage of the joint is essential if function is to be maintained. The steps in treatment are: 1. Open drainage by means of arthrotomy. 2. Fixation of the involved joint by some form of splint. 3. Traction to overcome muscle spasm. Only very severe cases of gonorrheal arthritis require drainage. Early results from fever therapy are very encouraging. O.M.S.

Common Painful Lesions of the Back.

Wm. J. Gardiner. Bull. Acad. Med. Toronto. 1936, **9**, 145.

The correct diagnosis and treatment of the common symptom, pain in the back, is not usually difficult if a good history is obtained, a thorough general and local physical examination is performed, and the various structures likely to be involved kept clearly in mind. General examination may reveal adequate cause for the symptom in any of the following: prostratic disease, pelvic inflammation, displacements and tumours of the uterus, ovarian cysts, acute nephritis, influenza, poliomyelitis, and others. Local examination may reveal the cause to be involvement of the spine, the ligaments or the musculature of the back. "Lumbago" is acute myofibrositis, successfully treated by diathermy, massage and graduated exercises. "Acute arthritis" is usually an exacerbation of osteoarthritis and in its acute stage requires rest on a firm mattress. This disease is a common cause of referred pain, particularly sciatica. Partial dislocations of lateral articular processes are most common in the cervical region, of sudden onset, and respond dramatically to manipulation. Partial dislocation of the sacro-iliac joint is frequently diagnosed "sprain." Sprains follow sudden, unusual strains on the back and, as in other joints, are characterized by tearing of ligaments, haemorrhage and exudation. The treatment to be avoided is prolonged immobilization favouring the formation of adhesions. Physiotherapy offers varied treatment for the conditions mentioned above in massage, diathermy, short wave therapy, manipulation and graduated exercises. Fracture, new growth and tuberculosis are always to be kept in mind. Any X-ray examination should include lateral as well as anterio-posterior views. Last of all are neuroses with pain in the back as a manifestation. Even this has a minor organic lesion as its basis in a large percentage of cases. B.H.M.